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(54) Title: NF-KB ACTIVATING GENE

(54) 発明の名称: N F- K B 活性化遺伝子

(57) Abstract: A protein having an NF-kB effect to be used in, for example, diagnosing, treating or preventing diseases in which the excessive activation or inhibition of NF-kB participate. From a cDNA library prepared from human lung fibroblasts, etc., a cDNA encoding a protein having an effect of activating NF-kB is cloned by using a plasmid pNF-kB-Luc and its DNA sequence and an amino acid sequence deduced therefrom are determined. This protein, DNA encoding the same, a recombinant vector containing this DNA and a transformant having this recombinant vector are usable in screening an NF-kB activation inhibitor or promoter.

(57) 要約:

NF-κBの過剰な活性化または阻害が関与する疾患の診断、治療または予防 等に使用されるΝFーκΒ作用を有するタンパク質の提供する。

ヒト肺線維芽細胞等から作製したcDNAライブラリーから、プラスミドpN FκΒーLucを用いて、NFーκΒを活性化する作用を有するタンパク質をコ ードするcDNAをクローニングして、そのDNA配列およびそれより推定され るアミノ酸配列を決定した。同タンパク質、これをコードするDNA,同DNA を含有する組換えベクターおよび同組換えベクターを含有する形質転換体は、N F-κBの活性化を阻害または促進する物質のスクリーニングに使用される。

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明 細 書

NF-κB活性化遺伝子

技術分野

本発明は、NF- κ Bを活性化する作用を有するタンパク質、該タンパク質をコードするDNA、該DNAの取得方法、該DNAを含有する組換えベクター、該組換えベクターを含有する形質転換体ならびに該タンパク質と特異的に反応する抗体に関する。また、本発明は、NF- κ Bの過剰な活性化または阻害が関与する疾患の診断、治療または予防を行う際の本発明のタンパク質、DNAまたは抗体の使用に関する。

また本発明は、該タンパク質、DNA、組換えベクターおよび形質転換体を用いて、NF $-\kappa$ Bの活性化を阻害または促進する物質をスクリーニングする方法に関する。

背景技術

転写因子NF- κ B(Nuclear factor kappa B)は、 炎症や免疫反応に関与する種々の遺伝子の転写調節において重要な役割を果たし ている。NF- κ Bは、Relファミリーに属するタンパク質のホモあるいはへ テロ二量体からなり、無刺激の状態では、制御タンパク質である $I\kappa$ B(Inhibitor of NF- κ B)と複合体を形成することによりその核移行シ グナルが覆い隠され、細胞質内で不活性型として存在する。

細胞にインターロイキン(IL)ー1、腫瘍壊死因子(TNF)ー α などのサイトカインの刺激が与えられると、I κ BはIKK(I κ B kinase)によってリン酸化され、ユビキチン化を経て26Sプロテアソームにより分解される。これにより遊離されたNF $-\kappa$ Bは核内に移行し、NF $-\kappa$ B結合配列と呼ばれているDNA配列に結合し、その制御下の遺伝子の転写を誘導する。NF $-\kappa$ Bによって発現調節を受けているとされている遺伝子は免疫グロブリン遺伝子の他、IL-1、TNF $-\alpha$ などの炎症性サイトカイン、インターフェロン、細

胞接着因子等が知られており、NF-κBはこれらの遺伝子の発現誘導を介して、 炎症や免疫応答に関わっている。

NF-кBの機能あるいは活性化を阻害することによって、炎症・免疫疾患やその他の疾病、たとえば腫瘍増殖、に関与している多くの因子(タンパク質)の発現を抑制できる可能性があり、自己免疫や炎症を原因・症状とする疾病に対する医薬の有望な標的である〔たとえば、Clinical Chemistry 45,7-17(1999)、J. Clin. Pharmacol. 38,981-993(1998)、Gut 43,856-860(1998)、The New England Journal of Medicine 366,1066-1071(1997)、TiPS 46-50(1997)、The FASEB Journal 9,899-909(1995)、Nature 395,225-226(1998)、Science 278,818-819(1997)、Cell 91,299-302(1997)。

細胞外からの情報は、何らかのシグナルの形に変えて、細胞膜を通過し細胞質をこえて核に到達し、標的遺伝子の発現を調節して細胞の応答が引き起こされる。そのため、細胞外の刺激からNF- κ Bの活性化に至る細胞内におけるシグナル伝達の仕組みを解明することは、自己免疫疾患や炎症症状を呈する疾患に対する新たな医薬の開発あるいは治療法の開発に非常に重要な手段を提供することとなり、極めて重要な意義を有している。

しかしながら、細胞が一定の刺激を受けてからNF- κ Bの活性化に至るまでのシグナル伝達経路にはプロテインキナーゼなどの各種伝達分子が関わる多くのステップの存在が考えられ、従って、より効率的な創薬研究のためには、主要な役割を果たす伝達分子を明らかにした上でそれらに焦点をしぼった新しい薬物スクリーニング方法を確立することが望まれる。しかし、NF- κ Bの活性化のメカニズムは上記IKK、ユビキチン化酵素、26Sプロテアソームの他、TNFreceptor associated factor 2(TRAF2)やNF- κ B inducing kinase(NIK)などの幾つかのシグナル伝達分子が同定され、少しずつ解明されつつあるものの、いまだ不明な点が多く、新たなシグナル伝達分子の同定とより進んだNF- κ B活性化メカニズムの

解明が望まれていた。

発明の開示

本発明の課題は、上記のように有用なNF- κ Bを直接的、あるいは間接的に活性化する作用を有する新規な遺伝子、タンパク質を見出し、これを医薬、診断薬、医療の分野で利用する方法を提供することにある。即ち、NF- κ Bを活性化する作用を有する新規タンパク質、該タンパク質をコードするDNA、該DNAを含有する組換えベクター、該組換えベクターを含有する形質転換体、該タンパク質の製造方法、該タンパク質またはその部分ペプチドに対する抗体、該抗体の製造方法を提供する。

また、本発明は、該タンパク質、DNA、組換えベクターおよび形質転換体を用いて、NF $-\kappa$ Bの活性化を阻害または促進する物質をスクリーニングする方法、該スクリーニング用キット、該スクリーニング方法もしくはスクリーニング用キットを用いて得られるNF $-\kappa$ Bの活性化を阻害または促進する物質、該物質の製造方法、NF $-\kappa$ Bの活性化を阻害または促進する物質を含有している医薬などを提供する。

近年、生体内で発現している遺伝子を解析する手段として、cDNAの配列をランダムに解析する研究が活発に行われており、このようにして得られたcDNAの断片配列がEST(Expressed Sequence Tag、たとえばhttp//www.ncbi.nlm.nih.gov/dbEST)として、データベースに登録され公開されている。しかし、ESTは配列情報のみであり、その機能を推定することは困難である。また、ESTはUniGene(http//www.ncbi.nlm.nih.gov/UniGene)により整備され、これまでに約92000クラスターが登録されている。しかし、その多くは5、端ヌクレオチド配列を欠損しており、タンパク質翻訳開始部位を含まない。そのため、mRNAのコード領域の決定を前提とするタンパク質の機能解析、プロモーターの解析による遺伝子発現制御の理解といった遺伝子機能の解析に直結しているとは言いがたい。

一方、遺伝子の産物、すなわちタンパク質の機能を解明する方法の一つに、動物細胞を用いた一過性発現クローニング法がある(たとえば、実験医学別冊 遺

伝子工学ハンドブック)。この方法は、動物細胞発現ベクターを用いて作製した c DNAライブラリーを、動物細胞にトランスフェクションすることで機能的なタンパク質を直接発現させ、このタンパク質が細胞に及ぼす生物活性を指標として c DNAを同定、クローニングする方法である。この方法では、目的とするタンパク質産物に関する化学的情報(アミノ酸配列や分子量)をあらかじめ必要とせず、細胞内や培養液中に発現しているタンパク質の特異的生物活性を検出して c DNAクローンの同定を行うことができる。

この発現クローニングを効率良く行なうためには、cDNAライブラリーの作製方法を工夫する必要がある。なぜなら、従来より汎用されているcDNAライブラリー作製方法には幾つかの方法があるが(たとえばGubblerーHoffmanの方法:Gene 25(1983)オカヤマーバーグの方法:Mol. Cell. Biol. 2(1982))、これらの方法によって作製されたcDNAは、そのほとんどが5、末端ヌクレオチド配列を欠損したものであり、完全長(mRNAの全ヌクレオチド配列を含む)であることは稀であるからである。その理由は、mRNAからcDNAを作るのに使用する逆転写酵素が、完全長のcDNAを作る効率が必ずしも高くないからである。

さらに、遺伝子の機能解析を試みるに際しては、完全長 c DNAをクローニングし、そこからタンパク質を発現させることが必須の要件である。従って、全体のクローンの中で、完全長のものの割合が高いライブラリーを作製することが、発現クローニングを効率良く行なうために必要であった。

本発明者らは、上記課題を解決するために鋭意研究を重ねた結果、オリゴキャッピング法を用いて完全長 c D N A ライブラリーを作製し、293 - E B N A 細胞を用いた発現クローニング法による遺伝子機能アッセイ系を完成し、該アッセイ系によりN F - κ B を活性化する作用を有するタンパク質をコードする新規 D N A (c D N A) を単離することに成功した。この新規 D N A は、293 - E B N A 細胞内で発現させることによりN F - κ B の活性化を誘発した。この結果は、この新規 D N A が N F - κ B の活性化に関与するシグナル伝達分子であることを示しており、本発明を完成するに至った。

すなわち、本発明は

- (1) 以下の(a) または(b) の精製されたタンパク質。
- (a)配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかで表されるアミノ酸配列からなるタンパク質。
- (b)配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかにおいて1若しくは複数個のアミノ酸が欠失、置換若しくは付加されたアミノ酸配列からなり、かつNF-κBを活性化する作用を有するタンパク質。

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- (2) 上記(1)記載のタンパク質とその全長にわたり少なくとも95%のアミノ酸配列の同一性を有するタンパク質であり、かつNF- κ Bを活性化する作用を有する、精製されたタンパク質。
- (3) 以下の(a)または(b)のタンパク質をコードするヌクレオチド配列を包含する、単離されたポリヌクレオチド。
- (a)配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、4

7、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかで表されるアミノ酸配列からなるタンパク質。

- (b) 配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかにおいて1若しくは複数個のアミノ酸が欠失、置換若しくは付加されたアミノ酸配列からなり、かつNF-κBを活性化する作用を有するタンパク質。
- (4) 以下の(a)~(c)のいずれかのポリヌクレオチド配列を含む単離されたポリヌクレオチド。
- (a) 配列番号2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112、114、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、16

7、169、171、173、175、177または179のいずれかで表されるポリヌクレオチド配列。

- (b)(a)のポリヌクレオチド配列と相補的なポリヌクレオチド配列を有するポリヌクレオチドとストリンジェントな条件下でハイブリダイズし、かつNF-κBを活性化する作用を有するタンパク質をコードするポリヌクレオチド配列。
- (c) 配列番号2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、
- 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70,
- 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94,
- 96, 98, 100, 102, 104, 106, 108, 110, 112, 11
- 4, 116, 118, 120, 122, 124, 126, 128, 130, 13
- 2, 134, 136, 138, 140, 142, 144, 146, 148, 15
- 0、151、153、155、157、159、161、163、165、16
- 7、169、171、173、175、177または179のいずれかにおいて、
- 1若しくは複数個のヌクレオチド配列が欠失、置換若しくは付加されたポリヌクレオチド配列からなり、かつNF $-\kappa$ Bを活性化する作用を有するタンパク質をコードするポリヌクレオチド配列。
- (5) 上記 (3) 記載のポリヌクレオチドと全長にわたり少なくとも 95%以上の同一性を有し、かつ $NF-\kappa$ Bを活性化する作用を有するタンパク質をコードするポリヌクレオチド配列を包含する単離されたポリヌクレオチド。
- (6) 上記(4)記載のポリヌクレオチドと全長にわたり少なくとも95%以上の同一性を有し、かつNF-κBを活性化する作用を有するタンパク質をコードするポリヌクレオチド配列を包含する単離されたポリヌクレオチド。
- (7) 上記 (3) \sim (6) のいずれか 1 つに記載のポリヌクレオチドによりコードされる精製されたタンパク質。
- (8) 上記(3) \sim (6) のいずれか 1 つに記載のポリヌクレオチドを含有する組換えベクター。
- (9) 上記(8)に記載の組換えベクターを含む形質転換された細胞。
- (10) 上記(1) または(2) に記載のタンパク質が膜タンパク質である場

合における、上記(9)記載の細胞の膜。

(11) (a)上記(3)~(6)のいずれか1つに記載の単離されたポリヌクレオチドがコードするタンパク質を発現する条件下で該ポリヌクレオチドを含有する形質転換された細胞を培養し、

- (b) 培養物からタンパク質を回収する、
- ことを含む、タンパク質の製造方法。
- (12) (a) 個体のゲノムにおける上記(1)、(2) または(7) に記載の タンパク質をコードするヌクレオチド配列中の変異の存在または不存在を決定し、 および/または
- (b) 該個体に由来するサンプル中での該タンパク質の発現量を分析する、 ことを含む該個体における該タンパク質の発現または活性に関連した、該個体に おける疾病または疾病への感受性の診断方法。

上記方法において、好ましくは、発現するタンパク質の量が正常の2倍以上の 場合、あるいは2分の1以下の場合に病気であると診断する。

- (13) 以下の工程を含むNF- κ B活性化の阻害活性または促進活性ついて 化合物をスクリーニングする方法。
- (a) NF-κBを活性化するタンパク質をコードする遺伝子およびNF-κB の活性化に対応した、検出可能シグナルを提供しうる成分を細胞に提供する工程、
- (b) 該遺伝子が形質転換された細胞内で発現可能となる条件下で該形質転換された細胞を培養する工程、
- (c) 該形質転換された細胞と1あるいは複数個の候補化合物とを接触させる工程、
- (d) 検出可能なシグナルを測定する工程、および
- (e) 該検出可能なシグナルの測定により活性化剤化合物および/または阻害剤 化合物として単離もしくは同定する工程。

また、シグナルを正常より2倍以上増加させる化合物を活性化剤化合物として 単離または同定し、2分の1以下に減少させる化合物を阻害剤化合物として単離 または同定することが好ましい。

(14) 以下の工程を含む、医薬組成物を製造する方法。

(a) NF-κBを活性化する作用を有するタンパク質をコードする遺伝子、および検出可能なシグナルを提供しうる成分を細胞に提供する工程、

- (b) 該遺伝子が形質転換された細胞内で発現可能となる条件下で該形質転換された宿主細胞を培養する工程、
- (c) 該形質転換された宿主細胞と1あるいは複数個の候補化合物とを接触させる工程、
- (d) 検出可能なシグナルを測定する工程、
- (e) 該検出可能なシグナルの測定により活性化剤化合物および/または阻害剤 化合物を単離もしくは同定する工程、および
- (f) 単離または同定された化合物を医薬組成物として最適化する工程。

また、本発明においては、シグナルを正常より2倍以上増加させる化合物を活性化剤化合物として単離または同定し、2分の1以下に減少させる化合物を阻害剤化合物として単離または同定することが好ましい。

- (15) NF $-\kappa$ B活性化の阻害活性または促進活性について化合物をスクリーニングするためのキットであって、
- (a) NF- κ Bを活性化するタンパク質をコードする遺伝子、およびNF- κ Bの活性化後、検出可能なシグナルを提供しうる成分により形質転換された細胞、および
- (b) 検出可能なシグナルを測定するための試薬 を含むキット。
- (16) 上記(1)、(2)または(7)に記載のタンパク質に特異的に結合するモノクローナルあるいはポリクローナル抗体。
- (17) 上記(1)、(2) または(7) に記載のタンパク質を抗原あるいはエ ピトープ含有フラグメントとして非ヒト動物に投与することからなる、上記(1)、
- (2) または(7) 記載のタンパク質に特異的に結合するモノクローナルまたは ポリクローナル抗体の製造方法。
- (18) NF- κ Bの活性化タンパク質の発現を阻害する、上記(3) \sim (6) のいずれか1つに記載のポリヌクレオチドに相補的なアンチセンスオリゴヌクレオチド。

(19) 上記(1)、(2) または(7) 記載のタンパク質をコードするRNA の開裂により、NF- κ Bの活性化を阻害するリボザイム。

- (20) 炎症、自己免疫疾患、感染症、癌および骨疾患からなる群から選択される疾患の治療に有効な量の上記(13)記載の方法でスクリーニングされた化合物および/または上記(16)記載のモノクローナルまたはポリクローナル抗体および/または上記(18)記載のアンチセンスオリゴヌクレオチドおよび/または上記(19)記載のリボザイムを個体に投与することを含む疾患の治療法。
- (21) NF- κ Bの活性化を阻害または活性化するものとして上記(14)に記載の方法により製造された医薬組成物。
- (22) 炎症、自己免疫疾患、癌、感染症、骨疾患、AIDS、神経変性疾患、 または虚血性障害の治療のための上記(21)記載の医薬組成物。
- (23) NF-κBに関連する疾患を患っている患者に上記(14)記載の方法により製造された医薬組成物を投与することからなる炎症、自己免疫疾患、癌疾患、感染症、骨疾患、AIDS、神経変性疾患、または虚血性障害を治療する方法。
- (24) 上記(16)記載のモノクローナルまたはポリクローナル抗体を有効 成分として含有する医薬組成物。
- (25) 上記(18)記載のアンチセンスオリゴヌクレオチドを有効成分として含有する医薬組成物。
- (26) 対象疾患が炎症、自己免疫疾患、感染症、癌疾患、骨疾患、AIDS、神経変性疾患および虚血性障害からなる群から選択される、上記(24)または(25)に記載の医薬組成物。
- (27) 機能を有する新規遺伝子の取得方法であり、少なくとも以下の工程を 含む方法。
 - (a) オリゴキャッピング法を用いて完全長 c D N A ライブラリーを作製し、
- (b) 完全長 c D N A および該機能を有するタンパク質の存在を示すシグナルを発する因子を含有するプラスミドを細胞中にコトランスフェクションし、さらに
 - (c) シグナルを発するプラスミドを選択する。
 - 尚、本発明における機能を有する新規遺伝子とは、例えば生物活性を持つタン

パク質をコードする核酸分子が挙げられる。

(28)配列番号2、4、6、8、10、12、14、16、18、20、2 2, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 4 6, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 7 0, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 9 4, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167、169、171、173、175、177および179で表されるヌク レオチド配列のうち少なくとも1以上を含むデータセットおよび/または配列番 号1、3、5、7、9、11、13、15、17、19、21、23、25、2 7, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 5 1, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 7 5, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 9 9, 101, 103, 105, 107, 109, 111, 113, 115, 11 7, 119, 121, 123, 125, 127, 129, 131, 133, 13 5, 137, 139, 141, 143, 145, 147, 149, 152, 15 4, 156, 158, 160, 162, 164, 166, 168, 170, 17 2、174、176、178および180で表されるアミノ酸配列のうち少なく とも1以上を含むデータセットを保存したコンピュータ読み込み可能媒体。

- (29) 上記(28)に記載の媒体上のデータと他のヌクレオチド配列および/ または他のアミノ酸配列のデータを比較して他のポリヌクレオチド配列および/ またはアミノ酸配列との同一性の算出を行う方法。
- (30)
 配列番号2、4、6、8、10、12、14、16、18、20、22,

 24、26、28、30、32、34、36、38、40、42、44、46、

 48、50、52、54、56、58、60、62、64、66、68、70、

 72、74、76、78、80、82、84、86、88、90、92、94、

 96、98、100、102、104、106、108、110、112、11

4、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、167、169、171、173、175、177または179から選択されるヌクレオチド配列の全てまたは一部を含むポリヌクレオチドが固定されている不溶性基質。

(31) 配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180で表されるアミノ酸配列から選択されるアミノ酸配列の全てまたは一部を含むポリペプチドが固定されている不溶性基質。

本明細書は本願の優先権の基礎である日本国特許出願 2000-402288 号、2001-088912 号及び 2001-254018 号、並びに、米国仮出願 60/258,315 号、60/278,640 号及び 60/314,385 号の明細書及び/または図面に記載される内容を包含する。

図面の簡単な説明

図1は、実施例3配列番号5のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。図中で横軸は、MG-132濃度、縦軸は、MG-132無添加(0μ M)条件での相対ルシフェラーゼ活性値を100%とした相対値を示す(各濃度での相対ルシフェラーゼ活性値をMG-132無添加条件での相対ルシフェラーゼ活性で割ってパーセント表示した)。

図2は、実施例3配列番号9のプロテアソーム阻害剤MG-132によるNF-κBのレポーター活性抑制を示す図である。

図3は、実施例3配列番号17のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図 4 は、実施例 3 配列番号 2 1 のプロテアソーム阻害剤MG-1 3 2 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図 5 は、実施例 3 配列番号 3 5 のプロテアソーム阻害剤MG-1 3 2 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図 6 は、実施例 3 配列番号 3 7 のプロテアソーム阻害剤MG-1 3 2 による N $F-\kappa$ B のレポーター活性抑制を示す図である。

図 7 は、実施例 3 配列番号 4 1 のプロテアソーム阻害剤MG-1 3 2 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図 8 は、実施例 3 配列番号 5 3 のプロテアソーム阻害剤MG-1 3 2 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図 9 は、実施例 3 配列番号 5 7 のプロテアソーム阻害剤MG-1 3 2 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図10は、実施例3配列番号63のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図11は、実施例3配列番号67のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図 1 2 は、実施例 3 配列番号 7 1 のプロテアソーム阻害剤MG-1 3 2 による $NF-\kappa B$ のレポーター活性抑制を示す図である。

図13は、実施例3配列番号75のプロテアソーム阻害剤MG-132による $NF-\kappa B$ のレポーター活性抑制を示す図である。

図 14 は、実施例 3 配列番号 81 のプロテアソーム阻害剤MG-132 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図 15 は、実施例 3 配列番号 87 のプロテアソーム阻害剤MG-132 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図16は、実施例3配列番号91のプロテアソーム阻害剤MG-132による

 $NF - \kappa B$ のレポーター活性抑制を示す図である。

図17は、実施例3配列番号93のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図 18 は、実施例 3 配列番号 97 のプロテアソーム阻害剤MG-132 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図19は、実施例3配列番号121のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図20は、実施例3配列番号123のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図21は、実施例3配列番号129のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図22は、実施例3配列番号154のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図23は、実施例3配列番号158のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図 24 は、実施例 3 配列番号 162 のプロテアソーム阻害剤MG-132 による $NF-\kappa$ B のレポーター活性抑制を示す図である。

図 2.5 は、実施例 3 配列番号 1.6 8 のプロテアソーム阻害剤MG-1.3 2 による $NF-\kappa$ B の V ポーター活性抑制を示す図である。

図26は、実施例3配列番号170のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図27は、実施例3配列番号172のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図28は、実施例3配列番号176のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

図29は、実施例3配列番号178のプロテアソーム阻害剤MG-132による $NF-\kappa$ Bのレポーター活性抑制を示す図である。

配列表の説明

配列番号181はプライマーである。 配列番号182はプライマーである。

発明を実施するための形態」

まず、本発明の基本的特徴を更に明らかにするために、本発明の完成に至る経 緯を追いながら、本発明について説明する。NF-κΒを活性化する作用を有す る新規遺伝子を取得する目的で、実施例に示すように、以下の実験を実行した。 まずヒト正常肺線維芽細胞(三光純薬株式会社より購入)より調製したmRNA より、オリゴキャッピング法によって完全長cDNAを作製し、該cDNAをベ クターpME18S-FL3 (GenBank Accession AB009864) に組み込んだ完全 長cDNAライプラリーを作製した。次に、該cDNAライブラリーを大腸菌に 導入し、1クローンずつプラスミドを調製した。次に、293ーEBNA細胞 (イ ンビトロジェン社)に、ルシフェラーゼをコードする DNA を含有する p N F κ B ーLucレポータープラスミド(STRATAGENE社)と上記の完全長 c D NAプラスミドとを共導入した。そして、24時間あるいは48時間培養後、ル シフェラーゼ活性を測定し、ルシフェラーゼ活性が対照実験(完全長cDNAの 代わりに、ベクターpME18S-FL3を入れた細胞)と比べて有意に上昇し ている(対照実験と比べてルシフェラーゼ活性が5倍以上の値を示した)プラス ミドを選抜し、該プラスミドにクローニングされているcDNAの全ヌクレオチ ド配列を決定した。このようにして得られたcDNAによりコードされるタンパ ク質は、該タンパク質がNFーκΒの活性化に関与するシグナル伝達分子である ことを示している。

次に、以下に本発明について詳細に説明する。

本発明におけるNF $-\kappa$ Bを活性化する作用を有するとは、適切な細胞内に遺伝子を導入し、該遺伝子にコードさせるタンパク質を過剰発現させた時、NF $-\kappa$ Bが直接的あるいは間接的に活性化される(NF $-\kappa$ Bの活性化を誘発する)ことをいう。NF $-\kappa$ Bの活性化は、例えば、NF $-\kappa$ B依存レポーター遺伝子を用いたアッセイにより測定できる。アッセイは、該レポーター活性を対照細胞(ベクターのみを導入した細胞)に比し上昇させる作用を有することをいう。レ

ポーター活性の上昇は、好ましくは、1.5倍以上、さらに好ましくは、2倍以上、さらに好ましくは5倍以上である。

レポーター活性は、発現させたいタンパク質をコードするポリヌクレオチド(例 えば c DNA) を適切な発現ベクター内にクローニングし、該発現ベクターとN F-κ B依存レポータープラスミドを適切な細胞に共導入 (コ・トランスフェク ション)し、一定時間培養後、レポーターの活性を測定することにより測定する ことができる。適切な発現ペクターは当業者にはよく知られており、例えば、p ME18S-FL3、pcDNA3. 1 (Invitrogen社) などが挙げ られる。レポーター遺伝子は、当業者がその発現を容易に検出できるものであれ ばよく、例えば、ルシフェラーゼ、クロラムフェニコールアセチルトランスフェ ラーゼ、βーガラクトシダーゼをコードする遺伝子である。ルシフェラーゼをコ ードする遺伝子を使用することが最も好ましく、NF-κB依存レポータープラ スミドとしては、例えば、pNF-κB-Luc (STRATAGENE社) が 例示される。適切な細胞とは、IL-1あるいはTNF-lphaなどの刺激によりNF-κBが活性化される応答を示すような細胞であり、例えば、293-EBN A細胞が挙げられる。細胞培養および細胞への遺伝子導入(トランスフェクショ ン)は、当業者であれば当該技術分野で公知の慣用方法により実施でき最適化で きる。

好ましい方法としては、293-EBNA細胞を細胞培養用96穴プレートに 1×10⁴ cells/wellom細胞数となるように、5%FBS (Fetal Bovine Serum) 存在下のDMEM (Dulbecco's Modified Eagle Medium) 培地にまき、5%CO₂存在下、37℃で24時間培養した後、FuGENE6 (Roche社)を用いて、pNF-κB-Lucレポータープラスミド (STRATAGE NE社)と、発現ベクターを1ウエルに共導入する。37℃で24時間培養後、ロングタームルシフェラーゼアッセイシステムピッカジーンLT2.0 (東洋インキ社)を用いて、ルシフェラーゼ活性を測定することによりNF-κBの活性化を測定する。ルシフェラーゼ活性の測定は、例えば、PerkinElmer社のWallac ARVOTMST 1420 MULTILABEL COUNTERを用いて測定できる。FuGENE6による遺伝子導入の方法及びピッカ

ジーンLT2.0によるルシフェラーゼ活性測定は、それぞれに添付されているプロトコールに従い実施できる。FuGENE6を用いた96穴プレートでの遺伝子導入の方法は、1ウエルあたり、FuGENE6の量は0.3 \sim 0.5 μ 1が良く、好ましくは0.3 μ 1であり、pNF $-\kappa$ B-Lucプラスミドの量は $50\sim100$ ngが良く、好ましくは50ngであり、発現ベクターの量は、 $50\sim100$ ngが良く、好ましくは100ngである。NF $-\kappa$ Bを活性化する作用を有するとは、該レポーター活性(ルシフェラーゼ活性)を対照実験(空のベクターのみを導入した細胞)に比し、上昇させる作用を有することをいう。レポーター活性の上昇は、好ましくは1.5倍以上、さらに好ましくは5倍以上である。

配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかのアミノ酸配列に関連して、本発明は、以下のタンパク質を提供する。

- (a) 上記アミノ酸配列を含むタンパク質。
- (b)上記アミノ酸配列の1つを有するペプチド。
- (c) NF $-\kappa$ Bを活性化し、かつ上記アミノ酸配列において、1 以上のアミノ酸の削除、置換または付加を有するタンパク質。
- (d) その全長にわたり配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、1

11、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のアミノ酸配列に少なくとも95%、好ましくは97~99%の同一性を有するアミノ酸配列を含むタンパク質。

"同一性"とは、当該技術で知られているとおり、配列を比較することにより 決定される、2以上のタンパク質あるいは2以上のポリヌクレオチドの間の関係 である。当該技術で"同一性"とは、タンパク質またはポリヌクレオチド配列の 間の適合によって、あるいは場合によっては、一続きのそのような配列間の適合 によって決定されるような、タンパク質またはポリヌクレオチド配列の間の配列 相関性の程度を意味する。"同一性"および"類似性"は、既知の方法により容易 に決定できる。同一性を決定する好ましい方法は、試験する配列間で最も長く適 合するように設計される。同一性および類似性を決定するための方法は、公に利 用可能なプログラムにコードされている。相同性決定には、Altschul らによる BLAST (Basic Local Alignment Search Tool) プログラム (たとえば、Altschul SF, Gish W, Miller W, Myers EW, Lipman DJ., J. Mol. Biol., 215: p403-410 (1990), Altschyl SF, Madden TL, Schaffer AA, Zhang J, Miller W, Lipman DJ., Nucleic Acids Res. 25: p3389-3402 (1997))を利用し決定することができる。BLAST のよ うなソフトウェアを用いる場合、デフォルト値を用いるのが好ましい。BLAST 検 索に一般的に用いられる主な初期条件は、以下の通りであるが、これに限定され ない。

アミノ酸置換行列とは20種類のアミノ酸の各々のペアの類縁性を数値化した行列であり、通常 BLOSUM62 のデフォルトマトリックスが用いられる。このアミノ酸置換行列の理論については Altschul S.F., J. Mol. Biol., 219:555-565 (1991) に、DNA 配列の比較への適用については States D. J., Gish W., Altschul S.F., Methods, 3:66-70 (1991) に示されている。その際の最適なギャップコストは経験的に決定されており、BLOSUM62 の場合は好ましくは、Existence 11、Extension 1のパラメーターが用いられる。期待値 (EXPECT) とは、データベース配列に対し

てマッチする際の統計的有意性に関する閾値であり、デフォルト値は10である。一例として、配列番号2のアミノ酸配列に対して例えば95%以上の同一性を有するタンパク質は、そのアミノ酸配列が配列番号2のアミノ酸配列のアミノ酸100個あたり5個までのアミノ酸の変化を含んでよいことを意味する。言い換えれば、対照アミノ酸配列に対して95%以上のアミノ酸配列の同一性を有するタンパク質は、対照配列中の全アミノ酸の5%までの数のアミノ酸が欠失または他のアミノ酸と置換していてもよく、あるいは、対照配列中の全アミノ酸配列のうち5%までの数のアミノ酸が対照配列中に挿入されたものであっても良い。対照配列におけるこれらの変化は、対照アミノ酸配列のアミノ末端またはカルボキシ末端位置に存在していてもよく、あるいはそれらの末端間のいずれかの位置に存在していてもよく、あるいは対照配列内で1個またはそれ以上の一連の群をなしていてもよい。

上記した配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかに記載されたアミノ酸配列からなるタンパク質がNF-κBを活性化する作用を有することは、本願明細書実施例に記載の通りである。

配列番号2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112, 114、116、118、120、122、124、126、128、130、132、1

34、136、138、140、142、144、146、148、150、1 51、153、155、157、159、161、163、165、167、1 69、171、173、175、177または179のいずれかのポリヌクレオ チドに関連して、本発明は、また以下の単離されたポリヌクレオチドを提供する。

- (a) 上記配列に少なくとも95%、好ましくは97-99%の同一性を有する ヌクレオチド配列を含むポリヌクレオチド。
- (b) 上記配列のポリヌクレオチド。
- (c) 配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかのアミノ酸配列に少なくとも95%、好ましくは97~99%の同一性を有するアミノ酸配列を有するタンパク質をコードするヌクレオチド配列を有するポリヌクレオチド。

上記ヌクレオチド配列に含まれるヌクレオチド配列に同一またはほとんど同一なポリヌクレオチドは、本発明のタンパク質をコードする全長 c DNA及びゲノムクローンまたは上記配列に対応する相同性の高い他の遺伝子の c DNAまたはゲノムクローンを単離するためのハイブリダイゼーションプローブとして、または核酸増幅反応のためのプライマーとして使用してもよい。代表的には、これらのヌクレオチド配列は、上記配列に70%同一であり、好ましくは、80%同一であり、より好ましくは90%同一であり、最も好ましくは、95%同一である。プローブまたはプライマーは、一般的には少なくとも15ヌクレオチドを含有し、好ましくは30ヌクレオチドを含有し、50ヌクレオチドを含有してもよい。特に好ましいプローブは、30~50ヌクレオチドを有する。特に好ましいプライマーは、20~25ヌクレオチドを有する。

本発明のポリヌクレオチドは、DNAの形態(たとえば、cDNAおよびクローニングによって得られるか、あるいは合成的に生成されるゲノムDNAを含む)であってもよく、RNA(たとえばmRNA)の形態であってもよい。該ポリヌクレオチドは、二本鎖であっても、一本鎖であってもよい。二本鎖の場合は、二本鎖DNA、二本鎖RNAまたはDNA:RNAのハイブリッドであってもよい。一本鎖の場合は、センス鎖(コード鎖としても知られる)であっても、アンチセンス鎖(非コード鎖としても知られる)であってもよい。

当業者であれば、公知の方法を用いてこのタンパク質中のアミノ酸の置換など を適宜行い、配列番号1、3、5、7、9、11、13、15、17、19、2 1, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 4 5, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 6 9, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 9 3, 95, 97, 99, 101, 103, 105, 107, 109, 111, 1 13, 115, 117, 119, 121, 123, 125, 127, 129, 1 31, 133, 135, 137, 139, 141, 143, 145, 147, 1 49, 152, 154, 156, 158, 160, 162, 164, 166, 1 68、170、172、174、176、178または180のいずれかに記載 のアミノ酸配列を有するタンパク質と同様に NF-κB を活性化する作用を有する タンパク質を作製することが可能である。一つの方法としては、該タンパク質を コードするDNAに対して、慣用の突然変異誘発法を使用する方法がある。別の 方法としてはたとえば部位特異的変異法(たとえば宝酒造株式会社のMutan -Super Express Km キット)が挙げられる。また、タンパク 質のアミノ酸の変異は自然界においても生じうる。このようにアミノ酸の欠失、 置換、付加により配列番号1、3、5、7、9、11、13、15、17、19、 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69,71,73,75,77,79,81,83,85,87,89,91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129,

131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかのタンパク質に対してアミノ酸配列が変異した変異体であって、NF-κBを活性化する作用を有するタンパク質及び該タンパク質をコードするDNAも本発明に含まれる。変異の数は、好ましくは10まで、より好ましくは5まで、最も好ましくは3までが好ましい。

アミノ酸置換の例としては、保存的置換が好ましく、具体的には以下のグループ内での置換が挙げられる。(グリシン、アラニン)(バリン、イソロイシン、ロイシン)(アスパラギン酸、グルタミン酸)(アスパラギン、グルタミン)(セリン、トレオニン)(リジン、アルギニン)(フェニルアラニン、チロシン)。

当業者であれば、ハイプリダイゼーション技術などを用いて配列番号1、3、 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79,81,83,85,87,89,91,93,95,97,99,101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176、178または180のいずれかで表されるアミノ酸配列からなるタンパ ク質をコードするDNA(たとえば配列番号2)またはその一部を基に、これと 類似性の高いDNAを単離して、該DNAから配列番号1、3、5、7、9、1 1, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 3 5, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 5 9, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 8 3, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 10 5, 107, 109, 111, 113, 115, 117, 119, 121, 12 3, 125, 127, 129, 131, 133, 135, 137, 139, 14

1, 143, 145, 147, 149, 152, 154, 156, 158, 16 0, 162, 164, 166, 168, 170, 172, 174, 176, 17 8または180で表されるアミノ酸配列からなるタンパク質と同様に NF-κB を 活性化する作用を有するタンパク質を得ることも通常行い得ることである。この ように上記した配列番号1、3、5、7、9、11、13、15、17、19、 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69,71,73,75,77,79,81,83,85,87,89,91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168、170、172、174、176、178または180のいずれかで表 されるアミノ酸配列のタンパク質と高い同一性を有するタンパク質であって、N F-κBを活性化する作用を有するタンパク質も本発明のタンパク質に含まれる。 高い同一性とは、上記配列番号1、3、5、7、9、11、13、15、17、 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67、69、71、73、75、77、79、81、83、85、87、89、 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 1 11, 113, 115, 117, 119, 121, 123, 125, 127, 1 29, 131, 133, 135, 137, 139, 141, 143, 145, 1 47, 149, 152, 154, 156, 158, 160, 162, 164, 1 66、168、170、172、174、176、178または180のいずれ かであらわされるアミノ酸配列の全長にわたり少なくとも90%、好ましくは9 5%、さらに好ましくは、少なくとも97以上の同一性を有するアミノ酸配列を 示す。

本発明のタンパク質としては、ヒトや哺乳動物のあらゆる細胞や組織に由来する天然のタンパク質でもよく、化学合成タンパク質であってもよく、また遺伝子

組換え技術によって得られたタンパク質でもよい。タンパク質は糖鎖やリン酸化などの翻訳後修飾は受けていても受けていなくても良い。

本発明は、上記で示される本発明のタンパク質をコードするポリヌクレオチド である。上記の配列番号1、3、5、7、9、11、13、15、17、19、 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168、170、172、174、176、178または180のいずれかで表 されるアミノ酸配列からなるタンパク質をコードするヌクレオチド配列としてよ り具体的には、たとえば配列番号2、4、6、8、10、12、14、16、1 8, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 4 2, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 6 6, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 9 0, 92, 94, 96, 98, 100, 102, 104, 106, 108, 11 0, 112, 114, 116, 118, 120, 122, 124, 126, 12 8, 130, 132, 134, 136, 138, 140, 142, 144, 14 6, 148, 150, 151, 153, 155, 157, 159, 161, 16 3、165、167、169、171、173、175、177または179の いずれかで表されるヌクレオチド配列が挙げられる。DNAはcDNAのほか、 ゲノムDNA、化学合成DNAも含まれる。遺伝暗号の縮重に従い、遺伝子から 生産されるタンパク質のアミノ酸配列を変えることなく配列番号1、3、5、7、 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 3 3, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 5 7, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 8 1, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103,

105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかで表されるアミノ酸配列からなるタンパク質をコードするヌクレオチド配列の少なくとも1つのヌクレオチドを他の種類のヌクレオチドに置換することができる。従って、本発明のDNAはまた、遺伝暗号の縮重に基づく置換によって変換されたヌクレオチド配列も含有する。このようなDNAは、公知の方法により合成することができる。

本発明のDNAは、配列番号2、4、6、8、10、12、14、16、18、 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44,46,48,50,52,54,56,58,60,62,64,66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165、167、169、171、173、175、177または179のいず れかで表されるヌクレオチド配列からなるDNAとストリンジェントな条件下で ハイブリダイズし、かつ $NF-\kappa$ Bを活性化する作用を有するタンパク質をコー ドするDNAも含まれる。ストリンジェントな条件とは、当業者には十分理解で きることであり、たとえば、T. Maniatisらの実験操作書 (Molec ular Cloning A Laboratory Manual, Col Spring Harbor Laboratory 1982,1989) に従えば容易に実施できる。

すなわち、ストリンジェントな条件とは、30%ホルムアミドを含むハイブリダイゼーション溶液中($5\times SSC$ (0.75MのNaCl、75mMのクエン酸三ナトリウム)、 $5\times$ デンハルト溶液、0.5% SDS、 100μ g/mlの変性せん断サケ精子DNA)で37%のインキュベーションを一晩行い、その後 2

 \times SSC、0.1%SDS中、室温で10分の洗浄を3回行い、次いで1 \times SSC、0.1%SDS中、37 $\mathbb C$ で10分の洗浄を2回行う条件である(低ストリンジエンシー)。より好ましい条件は、40%ホルムアミドを含むハイブリダイゼーション溶液中で42 $\mathbb C$ のインキュベーションを一晩行い、その後2 \times SSC、0.1%SDS中、室温で10分の洗浄を3回行い、次いで0.2 \times SSC、1%SDS中、42 $\mathbb C$ で10分の洗浄を2回行う条件である(中ストリンジエンシー)。最も好ましい条件は、50%ホルムアミドを含むハイブリダイゼーション溶液中で42 $\mathbb C$ のインキュベーションを一晩行い、その後2 \times SSC、0.1%SDS中、室温で10分の洗浄を3回行い、次いで0.2 \times SSC、0.1%SDS中、50 $\mathbb C$ で10分の洗浄を2回行う条件である(高ストリンジエンシー)。この際、得られたDNAは、NF $-\kappa$ Bを活性化する作用を有するタンパク質をコードすることが必須である。

本発明は、上記(3)あるいは(4)のポリヌクレオチドのヌクレオチド配列と高い類似性を有し、かつ NF- κ B を活性化する作用を有するタンパク質をコードするヌクレオチドを含むポリヌクレオチドを含む。代表的には、これらのヌクレオチド配列は、上記(3)または(4)のポリヌクレオチドのヌクレオチド配列の全長にわたり95%同一であり、より好ましくは97%同一であり、最も好ましくは少なくとも99%同一である。

上記の本発明のDNAは、前述のタンパク質を、組換えDNA技術を用いて製造するのに用いることができる。本発明のDNA及びペプチドは、概略以下のようにして得ることができる。

- (A) 本発明のタンパク質をコードするDNAをクローニングする。
- (B) タンパク質の全コード領域あるいはその一部をコードするDNAを発現用 ベクターに組み込んで、組換えベクターを構築する。
 - (C) 構築した組換えベクターにより、宿主細胞を形質転換する。
- (D) 得られた細胞を培養し、該タンパク質、またはその類縁体を発現させ、カラムクロマトグラフィーにより精製する。

上記の工程中でDNA、組換え体宿主としての大腸菌等の取り扱いに必要な一般的な操作は、当業者間で通常行われているものであり、たとえば、上記T. M

aniatisらの実験操作書に従えば容易に実施できる。使用する酵素、試薬類も全て市販の製品を用いることができ、特に断らない限り、製品で指定されている使用条件に従えば、完全にそれらの目的を達成することができる。以下に上記 $(A) \sim (D)$ の工程について更に詳しく説明する。

上記(A)における本発明のタンパク質をコードするDNAのクローニングの 手段としては、本願明細書実施例に記載した方法の他に、本発明のヌクレオチド 配列 (たとえば配列番号2、4、6、8、10、12、14、16、18、20、 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167、169、171、173、175、177または179のいずれか)の 一部を有する合成DNAをプライマーとしたPCR法によって増幅する方法、あ るいは、適当なベクターに組み込んだDNAを本発明のタンパク質の一部あるい は全領域をコードするDNA断片もしくは合成DNAを標識したものとのハイブ リダイゼーションによって選別すること、などが挙げられる。細胞、組織より全 RNAまたはmRNA画分を調製したものを用いて直接Reverse Tra nscriptase Polymerase Chain Reaction (RT-PCR法) によって増幅することもできる。 適当なべクターに組み込んだ DNAとしては、たとえば市販されている(CLONTECH社、STRATA GENE社)ライブラリーを使用することができる。ハイブリダイゼーションの 方法は、当業者間で通常行われているものであり、たとえば、上記T. Mani atisらの実験操作書に従えば容易に実施できる。クローン化された本発明の タンパク質をコードするDNAは目的によりそのまま、または所望により制限酵 素で消化したり、リンカーを付加したりして使用することができる。上記のよう にして得られるDNAは、配列番号2、4、6、8、10、12、14、16、

18、20、22,24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112,114、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、167、169、171、173、175、177または179のいずれかに記載のヌクレオチド配列を有する遺伝子であるか、あるいは前述の(3)~(6)のポリヌクレオチドであればよい。上記(B)において発現ベクターに組み込むDNAは、上述のタンパク質の全長をコードする全長cDNAでも、DNA断片でも良いし、その一部分を発現する様に構築されたDNA断片でも良い。

すなわち、本発明は、上記のDNAを含有する組換えベクターである。

本発明のタンパク質の発現ベクターは、たとえば、本発明のタンパク質をコードするDNAから目的とするDNA断片を切り出し、該DNA断片を適当な発現ベクター中のプロモーターの下流に連結することにより製造することができる。

用いる発現ベクターとしては、複製可能であれば、大腸菌をはじめとする原核生物由来、酵母由来、真菌由来、昆虫ウイルス由来、脊椎動物ウイルス由来いずれのベクターでも良いが、宿主として使用する微生物または細胞に適したものを選択する必要がある。また、発現物に応じて、宿主細胞―発現ベクター系としては、適切な組み合わせが選択される。

微生物を宿主として使用する場合、これら微生物に適したプラスミドベクター が組み換え体DNAの複製可能な発現ベクターとして一般に用いられる。

たとえば、大腸菌を形質転換するためのプラスミドベクターとしては、プラスミド pBR322やpBR327などを用いることができる。プラスミドベクターは通常複製起源、プロモーター、及び組換え体DNAで形質転換した細胞を選別するのに有用な表現型を組換え体DNAに与えるマーカー遺伝子等を含んでいる。プロモーターの例としては、β-ラクタマーゼプロモータ、ラクトースプロ

モーター、トリプトファンプロモーター等が挙げられる。マーカー遺伝子の例としては、アンピシリン耐性遺伝子やテトラサイクリン遺伝子などが挙げられる。 適した発現ベクターの例としては、プラスミドpBR322、pBR327の他に、pUC18、pUC19等が挙げられる。

酵母で本発明のDNAを発現するためには、複製可能なベクターとして、たとえばYEp24を用いることができる。プラスミドYEp24はURA3遺伝子を含有しており、このURA3遺伝子をマーカー遺伝子として利用することができる。酵母細胞用の発現ベクターのプロモーターの例としては、3ーホスホグリセレートキナーゼ、グリセルアルデヒドー3ーホスフェートデヒドロゲナーゼ、アルコールデヒドロゲナーゼなどの遺伝子のプロモーター等が挙げられる。

真菌で本発明のDNAを発現するための発現ベクターに用いられるプロモーター及びターミナーターの例としては、ホスホグリセレートキナーゼ (PGK)、グリセルアルデヒドー3ーホスフェートデヒドロゲナーゼ (GAPD)、アクチン等の遺伝子プロモーター及びターミネーターが挙げられる。適した発現ベクターの例としては、プラスミドpPGACY2、pBSFAHY83等が挙げられる。

昆虫細胞で本発明のDNAを発現させるための発現ベクターに用いられるプロ モーターの例としては、ポリヘドリンプロモーター、P10プロモーターなどが 挙げられる。

動物細胞で本発明のDNAを発現させるための組換えベクターは、一般に遺伝子を制御するための機能配列、たとえば、複製起源、本発明のDNAの上流に位置すべきプロモーター、リボソーム結合部位、ポリアデニル化部位や転写終止配列を含有している。本発明のDNAを真核細胞内で発現させるのに用いることができるそのような機能配列はウイルスやウイルス性物質から得ることができる。例えば、SR α プロモーター、SV40プロモーター、LTRプロモーター、CMV(サイトメガロウイルス)プロモーター、HSV-TKプロモーターなどがあげられる。これらのうち、CMVプロモーター、SR α プロモーターなどを用いるのが好ましい。また、本発明のタンパク質をコードする遺伝子の上流位置に本来存在するプロモーターも、上述の宿主ーベクター系で使用するのに適しているならば使用することができる。複製起源については、外来性の起源、たとえばア

デノウイルス、ポリオーマ、SV40等のウイルス由来の複製起点を用いることができる。また、発現ベクターとして宿主染色体に組み込まれるような性質を有するベクターを用いる場合、宿主染色体の複製起源を利用することができる。適した発現ベクターの例としては、プラスミドpSV-dhfr(ATCC=37146)、pBPV-1(9-1)(ATCC=37111)、pcDNA3.1(INVITROGEN社)、pME18S-FL3等が挙げられる。

本発明は、上記の組換えベクターを含む形質転換された細胞である。本発明の 複製可能な組換えベクターで形質転換された微生物または細胞は、前述の通り、 組換えベクターに与えられた少なくとも1種の表現型によって形質転換されずに 残った親細胞から選別される。表現型は少なくとも1種のマーカー遺伝子を組換 えベクターに挿入することによって与えることができる。また複製可能なベクタ ーが本来有しているマーカー遺伝子を利用することもできる。マーカー遺伝子の 例としては、たとえば、ネオマイシン耐性などの薬剤耐性遺伝子やジヒドロ葉酸 レダクターゼをコードする遺伝子などが挙げられる。

上記(C)において用いる宿主としては、大腸菌をはじめとする原核生物、酵母、真菌等の微生物、及び昆虫や動物等の細胞のいずれでも良いが、用いる発現ベクターに適したものを選択する必要がある。微生物の例としては、エシュリヒア コリ(Escherichia coli)の菌株、たとえばE.coli K12株294 (ATCC 31446)、E.coli X1776 (ATCC 31537)、E.coli C600、E.coli JM109、E.coli B株、あるいはバチラス サブチリス(Bacillus subtilis)の如きBacillus属の菌株、あるいはサルモネラ チフィムリウム(Salmonella typhimurium)またはセラチア マーゼサンス(Serratia marcesans)等の大腸菌以外の腸内菌、あるいはシュードモナス(Pseudomonas)属の種々の菌株が挙げられる。酵母としては、たとえば、サッカロミセス セレビシエ(Saccharomyces cerevisiae)、シゾサッカロマイセス ポンベ(Schizosacharomyces pombe)、ピキア パストリス(Pichia pastoris)などが用いられる。真菌としては、たとえば、アスペルギルス

ニドランス (Aspergillus nidulans)、アクレモニウム クリソゲナム (Acremonium chrysogenum) (ATCC 11550) 等が挙げられる。

昆虫細胞としては、たとえば、ウイルスがAcNPVの場合は、夜盗蛾の幼虫由来株化細胞(Spodoptera frugiperda:Sf細胞)、Trichoplusia niの卵由来のHigh FiveTM細胞、などが用いられる。動物細胞の例としては、HEK293細胞、COS-1細胞、COS-7細胞、Hela細胞、チャイニーズハムスター(CHO)細胞等が挙げられる。これらの中でも、CHO細胞およびHEK293細胞が好ましい。 細胞を宿主とする場合、用いられる発現ベクターと宿主細胞の組合せは実験の目的により異なるが、その組合せにより、一過的発現、構成的発現の2種類の発現方式が考えられる。

上記(C)における微生物及び細胞の形質転換とは、DNAを強制的方法や、 細胞の貪食能により微生物や細胞に取り込ませ、プラスミド状態あるいは染色体 に組み込まれた状態でDNAの形質を一過的あるいは構成的に発現させることで ある。当業者であれば公知の方法によって形質転換できる(たとえば実験医学別 冊遺伝子工学ハンドブック)。たとえば動物細胞の場合、DEAEーデキストラン 法、リン酸カルシウム法、エレクトロポレーション法(電気穿孔法)、リポフェク ション法などの方法でDNAを細胞に導入することができる。動物細胞を用いて、 本発明のタンパク質を安定に発現させる方法としては、上記の動物細胞に導入さ れた発現ベクターが染色体に組み込まれた細胞をクローン選択によって選択する 方法がある。具体的には、上記の選択マーカーを指標にして形質転換体を選択す る。さらに、このように選択マーカーを用いて得られた動物細胞に対して、繰り 返しクローン選択を行なうことにより本発明のタンパク質の髙発現能を有する安 定な動物細胞株を得ることができる。また、Dihydroforate re ductase (DHFR) 遺伝子を選択マーカーとして用いた場合Metho trexate(MTX)濃度を徐々に上げて培養し、耐性株を選択することに より、DHFR遺伝子とともに、本発明のタンパク質をコードするDNAを細胞 内で増幅させて、さらに高発現の動物細胞株を得ることもできる。

上記の形質転換された細胞を本発明のタンパク質をコードするDNAが発現可能な条件下で培養し、本発明のタンパク質を生成、蓄積せしめることによって、本発明のタンパク質を製造することができる。すなわち、本発明は、上記(3)~(6)に記載の単離されたポリヌクレオチドを含む形質転換された細胞を、該ポリヌクレオチドによりコードされているタンパク質を発現させる条件下培養し、次いで培養物から該タンパク質を回収することを含む該タンパク質の製造方法である。

上記の形質転換された細胞の培養は、当業者に公知の方法で行なうことができる(たとえばバイオマニュアルシリーズ4、羊土社)。たとえば動物細胞の場合、各種の動物細胞培養法、たとえば、シャーレ培養、マルチトレー式培養、モジュール培養などの付着培養、または細胞培養用担体(マイクロキャリアー)に付着させるか生産細胞自体を浮遊化させ浮遊培養等の公知の方法により培養を行なえば良い。培地は通常良く用いられる動物細胞用の培地、たとえばD-MEMやRPMI1640等を用いれば良い。

上記培養物から本発明のタンパク質を分離精製するには、自体公知の分離・精製法を適切に組み合わせて行なうことができる。これらの公知の分離、精製法としては、塩析や溶媒沈澱法などの溶解度を利用する方法、イオン交換クロマトグラフィーなどの荷電の差を利用する方法、透析法、限外ろ過法、ゲルろ過法、およびSDSーポリアクリルアミドゲル電気泳動法などの主として分子量の差を利用する方法、アフィニティークロマトグラフィーなどの特異的親和性を利用する方法、逆相高速液体クロマトグラフィーなどの疎水性の差を利用する方法、等電点電気泳動法などの等電点の差を利用する方法などが用いられる。たとえば、本発明のタンパク質は、硫安またはエタノール沈殿、酸抽出、アニオンまたはカチオン交換クロマトグラフィー、ホスフォセルロースクロマトグラフィー、疎水性相互作用クロマトグラフィー、アフィニティクロマトグラフィー、味水性相互作用クロマトグラフィーはよびレクチンクロマトグラフィーを含む既知の方法により組換え細胞培養物から回収し、精製することができる。最も好ましくは、高性能液体クロマトグラフィーが精製に使用される。ポリペプチドが細胞内合成、単離または精製の間に変性するときには、活性なコンフォーメションを再生する

ためにタンパク質をリフォールディングするためのよく知られた技術を使用できる。

本発明のタンパク質を他のタンパク質との融合タンパク質として製造することができる。これらも、本発明に含まれる。この融合タンパク質を発現する際に用いられるベクターとしては、該タンパク質をコードするDNAを組み込むことができ、かつ該融合タンパク質を発現することができるベクターであれば、いかなるベクターでも用いることができる。本発明のペプチドに融合できるタンパク質としては、たとえばグルタチオンーSートランスフェラーゼ(GST)、ヒスチジン残基の6個の連続配列(6×His)等が挙げられる。本発明のタンパク質を他の蛋白質と融合した蛋白質として発現させた場合には、融合した蛋白質に親和性をもつ物質を用いたアフィニティークロマトグラフィーを用いて精製することができ、有利である。例えば、GSTとの融合蛋白質として生産した場合は、グルタチオンをリガンドとするアフィニティークロマトグラフィーにより精製することができる。

本発明は、上記(7)のタンパク質の活性を阻害するタンパク質を含む。たと えば、抗体や上記(7)のタンパク質の活性中心等に結合し、活性の発現を妨げ る他のタンパク質が挙げられる。

本発明は、前記の本発明のタンパク質あるいはその部分ペプチドに特異的に結合する抗体ならびにそのような抗体の製造方法に関する。抗体は、本発明のタンパク質を認識し得る抗体であれば、ポリクローナル抗体、モノクローナル抗体、ならびにこれらの抗体のフラグメント、一本鎖抗体、ヒト化抗体の何れであってもよい。抗体フラグメントは、公知の技術によって作製することができる。たとえば、該抗体フラグメントには、限定されるものではないが、F(ab')2フラグメント、Fab'フラグメント、Fab'フラグメントが含まれる。たとえば、モノクローナル抗体またはポリクローナル抗体は、上記(1)または(2)に記載のタンパク質を抗原またはエピトープ含有フラグメントとして非ヒト動物に投与することにより得られる。本発明のタンパク質に対する抗体は、本発明のタンパク質あるいはそのペプチドを抗原として用い、自体公知の抗体または抗血清の製造法に従って製造することができる。たとえば実験医学別冊

新遺伝子工学ハンドプック 改訂第3版に記載の方法が挙げられる。

ポリクローナル抗体の場合であれば、たとえば、本発明のタンパク質をウサギなどの動物に本発明のタンパク質あるいはペプチドを注射することにより該タンパク質あるいはペプチドに対する抗体を産生させ、次いで血液を採取し、これを、たとえば硫安沈殿、イオン交換クロマトグラフィー、あるいは該タンパク質を固定化したアフィニティーカラム等によって精製することで調製することができる。

モノクローナル抗体の場合は、たとえば、本発明のタンパク質をマウスなどの動物に免疫し、同マウスから脾臓を抽出し、これをすりつぶして細胞にし、マウスミエローマ細胞とポリエチレングリコールなどの試薬により融合させ、これによりできた融合細胞(ハイブリドーマ)の中から、本発明のタンパク質に対する抗体を産生するクローンを選択する。次いで、得られたハイブリドーマをマウス腹腔内に移植し、同マウス内より腹水を回収し、得られたモノクローナル抗体を、たとえば硫安沈殿、イオン交換クロマトグラフィー、あるいは該タンパク質を固定化したアフィニティーカラム等によって精製することで調製することができる。

得られた抗体をヒトに投与する目的で使用する場合は、免疫原性を低下させるために、ヒト型化抗体あるいはヒト抗体を用いることが好ましい。ヒト型化抗体は、トランスジェニックマウスまたは他の哺乳動物を用いて作製することができる。これらのヒト型化抗体のやヒト抗体の一般的概説は、たとえば、Morrison, S. L. et al. [Proc. Natl. Acad. Sci. USA, 81:6851-6855(1984)]、Jones, P. T. et al. [Nature 321:522-525(1986)]、野口浩 [医学のあゆみ 167:457-462(1993)]、松本隆志 [化学と生物 36:448-456(1998)] によって供されている。ヒト化キメラ抗体は、マウス抗体のV領域とヒト抗体のC領域を遺伝子組換えにより結合し、作製することができる。ヒト化抗体は、マウスのモノクローナル抗体から相補性決定部位(CDR)以外の領域をヒト抗体由来の配列に置換することによって作製できる。また、免疫系をヒトのものと入れ換えたマウスを用いて、該マウスを免疫して、通常のモノクローナル抗体と同様に直接ヒト抗体を作製することもできる。これらの抗体は、タンパク質を発現するクローンを単離したり同定するのに使用できる。また、こ

れらの抗体は、本発明のタンパク質を細胞抽出液、または本発明のタンパク質を 産生する形質転換細胞から精製するのに使用できる。更にこれらの抗体は、細胞 や組織中の本発明のタンパク質を検出するELISAやRIA(ラジオイムノア ッセイ)、またはウエスタンブロット系の構築に使用できる。このような検出系は、 動物、好ましくは、ヒトの組織または血管内流体などの身体サンプル中に存在す る本発明のタンパク質の存在量を検出する診断目的に使用することができる。た とえば、これらの抗体は、炎症、自己免疫疾患、感染症(一例としてHIV感染)、 骨疾患、癌などの、本発明のタンパク質の(発現)異常に起因するΝF - κΒの望 ましくない活性化または抑制によって特徴付けられる疾患の診断に使用できる。 疾患の診断の基礎を提供するために、本発明のタンパク質の発現についての通常 の値、すなわち標準値が確立されなければならないが、これは当業者においては 周知の技術である。すなわち、複合体形成のための適切な条件下で、ヒトあるい は動物のどちらでもよいが、正常の被験者から得られた体液あるいは細胞抽出物 と、本発明のタンパク質に対する抗体とを結合させ、この抗体ータンパク複合体 の量を化学的または物理的手段により検出し、これを既知量の抗原(本発明のタ ンパク質)を含む標準液を用いて作成した標準曲線を用いて、正常サンプルから 得られた標準値を算出する。標準値と本発明のタンパク質が関係する疾患を潜在 的に患う被験者からのサンプルから得られた値と比較し、標準値との偏差によっ て疾病の存在を確認することができる。また、これらの抗体は、本発明のタンパ ク質の機能を研究する試薬としても用いることができる。

本発明の抗体は精製され得、次いで、たとえば、炎症、自己免疫疾患、感染症 (一例としてHIV感染)、癌などの、本発明のタンパク質の(発現)異常に起因するNF- κ Bの望ましくない活性化によって特徴付けられる疾患の患者に投与され得る。すなわち本発明は、上記に記載の抗体を有効成分として含有する医薬、および抗体を用いた治療方法である。これらの医薬は治療的使用のためにさらなる有効成分または不活性成分(たとえば、従来の薬学的に受容可能なキャリアまたは希釈剤(たとえば、免疫原性アジュバント)と、生理学的に無毒の安定化剤および賦形剤とともに組み合わされ得る。これらの組み合わせは、濾過滅菌され、そして凍結乾燥により投薬バイアル中に、または安定化水性調製物中の貯蔵物と

して投薬形態にされ得る。患者への投与は、たとえば、動脈内注射、静脈内注射、 皮下注射などの当業者に公知の方法により行い得る。投与量は、患者の体重や年 齢、投与方法などにより変動するが、当業者であれば適当な投与量を適宜選択す ることが可能である。これらの抗体は、本発明のタンパク質で仲介されるNF-、Bの活性化を阻害し、治療効果を示す。

本発明のDNAは、細胞内シグナリングプロセスに関与する他のタンパク質を単離、同定、クローン化することにも使用できる。たとえば、本発明のタンパク質をコードするDNA配列は、コードされたタンパク質を「バイト(bait)」として用いて、cDNAまたはゲノムDNAライブラリーから、本発明のタンパク質に結合できるタンパク質をコードする他の配列「プレイ(prey)」を単離し、クローン化する酵母ツーハイブリッドシステム(たとえばNature、340:245-246(1989))に用いることができる。同様の方式で、本発明のタンパク質が、他の細胞タンパク質(たとえばNIK, TRAF2)に結合できるかどうかも決定することができる。あるいは別の方法として、本発明のタンパク質の抗体を用いた免疫沈降法(たとえば、実験医学別冊新遺伝子工学ハンドブック)によって、本発明のタンパク質に結合し得るタンパク質を細胞抽出物から単離する方法が挙げられる。さらに別の方法として、上記に記載のように、本発明のタンパク質を他のタンパク質との融合タンパク質として発現させ、融合タンパク質に対する抗体を用いて免疫沈降法を行ない、本発明のタンパク質に結合し得るタンパク質に結合し得るタンパク質に結合し得るタンパク質に結合方法が挙げられる。

診断アッセイは、前述の方法により、NF - κBを活性化する機能を持つ(1)、

(2) または(7) のタンパク質遺伝子中の変異を検出することにより疾患の診断や該疾患への感受性を決定するための方法を提供する。さらに、このような疾患は、個体に由来するサンプル中のタンパク質またはmRNAレベルの異常な減少または増加を測定することを含む方法によって診断してもよい。発現の減少または増加は、当該技術でRNAレベルでのポリヌクレオチドの定量によく知られた方法、たとえば、RT-PCRなどの核酸増幅法、およびRNase保護法、ノーザンブロット法その他のハイブリダイゼーション法などの方法で測定できる。宿主に由来するサンプル中のタンパク質レベルの測定に使用され得るアッセイ技

術は、当業者によく知られている。そのような方法には、ラジオイムノアッセイ、 競合的結合測定法、ウェスタンプロット分析およびELISAアッセイが含まれ る。本発明のDNAは、本発明のタンパク質またはそのペプチドフラグメントを コードするDNAまたはmRNAにおける異常を検出するのに使用できる。本発 明は、個体における上記(1)、(2)または(7)に記載のタンパク質の発現に 関連した疾患または疾患への感受性を診断する方法に関する。該方法は、タンパ ク質をコードするポリヌクレオチド配列における変異を、測定することを含む。

本発明のDNAは、本発明のDNAを用いることによって、本発明のタンパク質またはその部分ペプチドをコードするDNAまたはmRNAの異常を検出することができるので、たとえば、該DNAまたはmRNAの損傷、突然変異あるいは発現低下や、増加あるいは発現過多などの遺伝子診断に有用である。すなわち本発明は、個体における該タンパク質の発現または活性に関連した、該個体における疾病または疾病への感受性の診断方法であって、

- (a) 個体のゲノムにおける請求項1、2または7に記載のタンパク質をコード するヌクレオチド配列中の変異の存在または不存在を決定し、および/または
- (b) 該個体に由来するサンプル中での該タンパク質の発現量を分析する、ことを含む診断方法であって、好ましくは発現するタンパク質の量が正常の2倍以上あるいは1/2以下の場合に病気であると診断する方法に関する。

上記(a)により、NF- κ Bを活性化する機能を持つ(1)、(2)または(7)のタンパク質をコードするヌクレオチド配列に変異がある場合は、該変異がNF- κ Bの活性化に関連した疾病を引き起こす可能性がある。あるいは、(b)により、被験者における前記(1)、(2)または(7)のタンパク発現量を測定し正常値を異なる値を示す場合は、NF- κ Bを活性化する作用を持つ本発明の新規タンパク質の発現量異常がNF- κ Bの活性化に関連した疾病の原因である可能性がある。ここで、(a)のNF- κ Bを活性化する機能を持つ(1)、(2)または(7)のタンパク質をコードするヌクレオチド配列の変異の有無を測定する方法としては、それちのタンパク質をコードする遺伝子のヌクレオチド配列の一部をプライマーとして、RT-PCRを行い、その後通常のヌクレオチド配列決定方法によって配列を決定し、変異の有無を検出できる。あるいは、PCR-SS

CP法(Genomics、5:874-879、1989年、実験医学別冊新 遺伝子工学ハンドブック)によっても変異の有無を調べることができる。

また、(b)のタンパク質発現量を調べる方法としては、たとえば、前記(16)に記載の抗体を利用する方法が挙げられる。

また、本発明は、本発明のタンパク質によるNF-κBの活性化を阻害または 促進する化合物のスクリーニング方法に関する。

このスクリーニング方法は、

- (a) NF-κBを活性化する作用を有するタンパク質をコードする遺伝子および検出可能なシグナルを提供し得る成分を細胞に提供する工程、
- (b) 該遺伝子が形質転換された細胞内で発現可能となる条件下で形質転換された宿主細胞を培養する工程、
- (c) 該形質転換された細胞と1あるいは複数個の被検化合物とを接触させる工程、
- (d) 検出可能なシグナルを検出する工程、および
- (e) 該検出可能なシグナルの測定により活性化剤化合物および/または阻害剤 化合物を離または同定する工程、

を含む。

また、シグナルを正常より2倍以上増加させる化合物を活性化剤化合物として 単離または同定し、2分の1以下に減少させる化合物を阻害剤化合物として単離 または同定することが好ましい。

検出可能なシグナルを提供し得る成分としては、たとえばレポーター遺伝子が 挙げられる。レポーター遺伝子は、テストを行なう転写因子の活性化を直接検出 するかわりに用いられるもので、調べたい遺伝子のプロモーターをレポーター遺 伝子につなぎ、レポーター遺伝子の産物の活性を測定することによってプロモー ターの転写活性の解析を行なうものである(バイオマニュアルシリーズ 4、羊土 社 (1994))。

レポーター遺伝子としては、その発現産物の活性または生産量(mRNAの生産量も含まれる)を当業者が測定可能なものであれば、いかなるペプチド、タンパク質をコードする遺伝子も用いることができる。たとえば、クロラムフェニコ

ールアセチルトランスフェラーゼ、 β ーガラクトシダーゼ、ルシフェラーゼ等の酵素活性を測定することで利用できる。 $NF-\kappa$ Bの活性化を評価するのに用いるレポータープラスミドとしては、 $NF-\kappa$ B認識配列をレポーター遺伝子の上流に組み込んだものであればよく、たとえば $pNF-\kappa$ BーLuc(STRAT AGENE社)が利用できる。あるいは、Tanaka S. et. al J. Vet. Med. Sci. Vol. 59 (7)、Rothe M. et. al. Science Vol. 269 p1424-1427 (1995) に記載の $NF-\kappa$ B依存レポータープラスミドが例示される。

宿主細胞としては、 $NF-\kappa$ Bの活性化を検出し得る細胞であればよく、好ましくは、哺乳動物細胞であり、たとえば293-EBNA細胞が好適に用いられる。形質転換及び培養に関しては、上記に記載の通りである。

NFーκ Βの活性化を阻害または促進する化合物のスクリーニングは、具体的 には、たとえば、一定時間培養した形質転換細胞に、被験物質を任意の量添加し、 一定時間後の該細胞が発現するレポーター活性を測定し、被験物質を添加しない 細胞のレポーター活性と比較することにより、NF-κBの活性化を阻害または 促進する化合物をスクリーニングすることができる。レポーター活性の測定は、 当業者に公知の方法 (たとえばバイオマニュアルシリーズ4、羊土社 (1994)) で行なうことができる。スクリーニングの被検物質には特に制限はなく、低分子 化合物、ペプチドなどが挙げられる。被検物質は、人工的に合成したものであっ ても、天然に存在するものであっても良い。また単一物質でも、混合物でもい。 検出可能なシグナルとしては、上記レポーター遺伝子の他に、NFーκ Βの活性 化によって発現が誘導されることが知られている、たとえばIL-1やTNFαのmRNA量あるいはタンパク質量を測定しても良い。mRNA量の測定は、 たとえばノーザンハイブリダイゼーションやRT-PCR法などが挙げられる。 タンパク質量の測定はたとえば抗体を用いる方法が挙げられる。抗体は公知の方 法によって作製しても良いし、市販のもの(たとえば和光純薬工業株式会社)を 使用することもできる。

また、以下の(a)~(f)の工程により医薬組成物を製造することも可能である。

(a) NF-κBを活性化する作用を有するタンパク質をコードする遺伝子および検出可能なシグナルを与えることができる成分を細胞に提供する工程、

- (b) 該遺伝子が形質転換された細胞内で発現可能となる条件下で形質転換された宿主細胞を培養する工程、
- (c) 該形質転換された宿主細胞と1あるいは複数個の化合物とを接触させる工程、
- (d) 検出可能なシグナルを測定する工程、
- (e) 該検出可能なシグナルの測定により活性化剤化合物および/または阻害剤 化合物を単離または同定する工程、および
 - (f) 単離または同定された化合物を医薬組成物として最適化する工程。

また、本発明においてシグナルを正常より2倍以上増加させる化合物を活性化 剤化合物、2分の1以下に減少させる化合物を阻害剤化合物として単離または同 定することが好ましい。

本願発明のタンパク質は、以下の工程により、該タンパク質のアゴニスト、アンタゴニストまたは阻害剤を、構造を基礎にして設計する方法に使用してもよい。

- (a)まず、タンパク質の三次元構造を決定する工程、
- (b) アゴニスト、アンタゴニストまたは阻害剤の反応性部位または結合部位と 思われる部位の三次元構造を推論する工程、
- (c)推論した結合部位または反応性部位に結合するかあるいは結合すると予測 される候補化合物を合成する工程、および
- (d) 該候補化合物が本当にアゴニスト、アンタゴニストまたは阻害剤であるか 否かを試験する工程。

また本発明は、上記スクリーニングによって得られた化合物を含む。しかしながら、本発明のスクリーニング方法は、上記の方法に限定されるものではない。 さらに、上記(14)に記載の方法により医薬組成物を製造する方法も含む。

該候補化合物には特に制限はなく、低分子化合物、ペプチドなどが挙げられ、また、人工的に合成したものであっても、天然に存在するものであっても良い。上記スクリーニングによって得られた化合物は、NF $-\kappa$ Bの活性化を阻害または促進する作用を有しているので、NF $-\kappa$ Bの望ましくない活性化あるいは不

活性化に起因する疾患を治療または予防するための医薬として有用である。混合 物から目的化合物を単離、精製するには、自体公知の方法、例えば濾過、抽出、 洗浄、乾燥、濃縮、結晶化、各種クロマトグラフィー等を適宜組み合わせて行な うことができる。化合物の塩を取得したい時は、化合物が塩の形で得られる場合 にはそのまま精製すれば良く、また遊離の形で得られる場合には、通常の方法に より適当な溶媒に溶解または懸濁し、所望の酸または塩基を添加し、塩を形成さ せて単離精製すれば良い。本発明の方法を用いて得られる化合物またはその塩を 医薬組成物として最適化する工程としては、例えば以下のような常法により製剤 化する方法が例示される。すなわち活性成分として有効な量の上記化合物または その薬理的に許容される塩と、薬理的に許容される担体とを混合すれば良い。製 剤化は選択された投与様式に適した形態が選ばれる。経口投与に適した組成物と しては、錠剤、顆粒剤、カプセル剤、丸剤、および散剤などの固体形態、溶液剤、 シロップ剤、エリキシル剤、および懸濁液剤などの液体形態が挙げられる。非経 口投与に有用な形態としては、無菌溶液剤、乳剤、および懸濁液剤が挙げられる。 上記の担体としては、例えばゼラチン、乳糖、グルコース等の糖類、コーン・小 麦・米・とうもろこし澱粉等の澱粉類、ステアリン酸等の脂肪酸、ステアリン酸 カルシウム・ステアリン酸マグネシウム等の脂肪酸塩、タルク、植物油、ステア リンアルコール・ベンジルアルコール等のアルコール、ガム、ポリアルキレング リコール等が挙げられる。これらのうち液状担体の例としては、一般に水、生理 食塩水、デキストロースまたは類似の糖溶液、エチレングリコール、プロピレン グリコール、ポリエチレングリコール等のグリコール類が挙げられる。

本発明は、NF-κB活性化の阻害活性または促進活性について化合物をスクリーニングするためのキットである。該キットは、

- (a) NF- κ Bを活性化する作用を有するタンパク質をコードする遺伝子およびNF- κ Bの活性化後、その活性化が検出可能なシグナルを提供する成分を含有する細胞、
- (b) 該検出可能なシグナルを測定するための試薬、から成り、NF-κBの活性化を阻害または促進する化合物をスクリーニングするために必要な試薬類を含む。

別の側面において、本発明は、

(a) 配列番号2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112、114、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、167、169、171、173、175、177または179で表されるヌクレオチド配列を有する本発明のポリヌクレオチド;

- (b)(a)のヌクレオチド配列に相補的なヌクレオチド配列;
- (c)配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180で表されるアミノ酸配列を有する本発明のタンパク質またはそれらの断片;または
- (d)(c)の本発明のタンパク質に対する抗体;

を含む診断キットに関する。

少なくとも(a)~(d)のいずれかを含むキットは、炎症、自己免疫疾患、 感染性疾患(たとえばHIV感染)および癌などの疾患または該疾患への感受性 を診断するのに有用である。

NF-κBは、炎症、自己免疫疾患、ガン及びウイルス感染などの多種の病理 学的状態におけるその関与のため、薬物デザイン及び治療介在のための魅力的な

標的である。多数の実験が、NF-κB活性が深い生理学的作用を有し得ること を示している (たとえば、Ann. Rheum. Dis. 57, 738-741 (1998), American Journal of Pathology 152, 793-803 (1998), ARTHRITIS & AMP; RHEUMATISM 40, 226-236 (1997), Am. J. Respir. Crit. Care Med. 158, 1585-1592 (1998), J. Exp. Med. 188 1739-1750 (1998), Gut 42, 477-484 (1998), The Journal of Immunology 161, 4572-4582 (1998), Nature Medicine 3,894-899 (1997))。本明細書中に報告する NF-κBを活性化する作用を有する新規タンパク質の発見により、異常なNF - κ B機能を制御する新しい方法が提供された。さらなる具体例において、本発 明は、 $NF-\kappa$ Bの活性化を阻害するための前記の $NF-\kappa$ Bを活性化する作用 を有するタンパク質の機能を阻害する化合物を用いる方法に関する。また、本発 明は、ΝΓ-κΒの活性化を促進するための前記のΝΓ-κΒを活性化する作用 を有するタンパク質の機能を活性化する化合物を用いる方法に関する。上記スク リーニング方法によって得られた、NF-κBの活性化を阻害する化合物は、た とえば炎症、自己免疫疾患(慢性関節リウマチ、全身性エリテマトーデス、喘息 など)、感染症、骨疾患、移植片拒絶反応などの、NF-κBの望ましくない活性 化によって特徴つけられる疾患を治療または予防する医薬として有用である。更 に、NF-κBの活性化が細胞のアポトーシスを抑制することが、最近明らかに なりつつある。上記スクリーニング方法によって得られた、NFーκ Bの活性化 を阻害する化合物は、アポトーシスを促進する機能を持つ可能性も考えられる。 アポトーシスの誘導が治療につながる疾患としては、腫瘍が挙げられる。

また、NF- κ B活性の異常に関連する疾患としては、例えば、AIDS (acquired immunodeficiency syndrome)、神経変性疾患(アルツハイマー病、パーキンソン病、筋萎縮性側索硬化症など)、虚血性障害(心筋梗塞、再潅流障害などにより起こるものなど)、骨髄形成不良症候群(再生不良性貧血など)、皮膚疾患(Toxic epidermal necrolysis など)、増殖性腎炎(IgA腎炎、紫斑病性腎炎、ループス腎炎)、劇症肝炎などが挙げられる。よって、上記スクリーニング方法によって得られた、NF- κ B活性化を阻害する化合物または促進する化合物はこれらの疾患の治療または予防のための医薬として有用である。

更に、本発明のタンパク質をコードする遺伝子は、癌、自己免疫疾患、アレル

ギー性疾患、および炎症性応答を初めとする様々な疾患の治療を目的とした遺伝子治療にも有用である。遺伝子治療とは、疾病の治療を目的として、遺伝子または遺伝子を導入した細胞をヒトの体内に投与することを意味する。本発明のタンパク質や該タンパク質をコードする DNA は、診断目的にも使用できる。

本発明のスクリーニング方法を用いて得られる化合物またはその塩を上述の医薬組成物として使用する場合、常套手段に従って実施することができる。たとえば、錠剤、カプセル剤、エリキシル剤、マイクロカプセル剤、無菌性溶液、懸濁液剤などとすることができる。このようにして得られる製剤は安全で低毒性であるので、たとえば、ヒトや哺乳動物(たとえば、ラット、ウサギ、ヒツジ、ブタ、ウシ、ネコ、イヌ、サルなど)に対して投与することができる。患者への投与は、たとえば、動脈内注射、静脈内注射、皮下注射など当業者に公知の方法により行いうる。投与量は、患者の体重や年齢、投与方法などにより変動するが、当業者であれば適当な投与量を適宜選択することが可能である。また、該化合物が DNAによりコードされうるものであれば、該 DNA を遺伝子治療用ベクターに組込み、遺伝子治療を行うことも考えられる。投与量、投与方法は、患者の体重や年齢、症状などにより変動するが、当業者であれば適宜選択することが可能である。すなわち本発明は、上記化合物を有効成分として含有する医薬に関する。

さらに、上記化合物は、炎症、自己免疫疾患、ウイルス性疾患、感染症、ガン、 骨疾患などの、NFー κ B活性の異常によって特徴つけられる疾患を治療または 予防する医薬として有用である。すなわち本発明は、上記化合物を含む炎症、自 己免疫疾患、ウイルス性疾患、感染症、ガン、骨疾患などの医薬に関する。具体 的には、例えば、慢性関節リウマチ、変形性関節症、全身性エリテマトーデス、 糖尿病、敗血症、喘息、アレルギー性鼻炎、虚血性心疾患、炎症性腸疾患、くも 膜下出血、ウイルス肝炎、エイズ、アテローム性動脈硬化症、アトピー性皮膚炎、 ウイルス感染症、クローン病、糖尿病、通風、肝炎、多発性硬化症、心筋梗塞、 腎炎、骨粗鬆症、アルツハイマー、パーキンソン病、ハンチントン舞踏病、乾癬、 筋萎縮性側索硬化症、心筋梗塞、再生不良性貧血などに対する治療及び予防薬と して有用である。

さらにまた、本発明は、炎症、自己免疫疾患、ウイルス性疾患、ガン、感染症、

骨疾患などの医薬の製造における上記(14)記載の方法により製造された医薬 組成物の使用も含む。 また本発明は、上記(3)~(6)に記載の遺伝子に対す るアンチセンスオリゴヌクレオチドである。アンチセンスオリゴヌクレオチドは、 標的とした遺伝子配列に対して相補的な配列を持つオリゴヌクレオチ ドを用いて、 タンパク質への翻訳、細胞質への輸送、あるいは全体的な生物活性機能に必要な 他の活性等のRNAの機能を阻害することによって、標的遺伝子の発現を抑制す ることができる。この際、アンチセンスオリゴヌクレオチドとしては、RNAを 用いても良いし、DNAを用いても良い。本発明のDNA配列は、本発明のタン パク質をコードする遺伝子から転写されたmRNAとハイプリダイズし得るアン チセンスオリゴヌクレオチドを作製するために使用できる。一般にアンチセンス オリゴヌクレオチドが、その遺伝子の発現に対して抑制的に作用することは公知 での事実である(たとえば、細胞工学 Vol. 13 No. 4 (1994))。本 発明のタンパク質をコードする遺伝子に対するアンチセンスコード配列を有する オリゴヌクレオチドは、標準の方法で細胞内に導入することができ、該オリゴヌ クレオチドは、本発明のタンパク質をコードする遺伝子のmRNAの翻訳を効果 的に遮断して、その発現を遮断して、望ましくない作用が阻害される。

本発明のオリゴヌクレオチドは、天然に見出されるオリゴヌクレオチドの他に、修飾されたものであっても良い [たとえば、村上&牧野:細胞工学 Vol. 13 No. 4 p 2 5 9 - 2 6 6 (1994)、村上章:蛋白質核酸酵素 Vol. 40 No. 10 p 13 6 4 - 13 7 0 (1995)、竹内恒成ら:実験医学 Vol. 40 No. 4 p 8 5 - 9 5 (1996)。従って、オリゴヌクレオチドは変化した糖部分あるいは糖間部分を有していても良い。これらの例は、当該技術分野において使用が知られているホスホチオエート及び他のイオウ含有種である。幾つかの好ましい態様に従えば、オリゴヌクレオチドの少なくとも一つのホスホジエステル結合が、その活性が調節されるべきRNAが位置する細胞の領域に浸透する組成物の能力を高める機能を有する構造により置換される。

このような置換は、ホスホロチオエート結合、ホスホロアミデート結合、メチルホスホネート結合または短鎖アルキルもしくはシクロアルキル構造を含むことが好ましい。オリゴヌクレオチドはまた、少なくとも幾つかの修飾されたヌクレ

オチド型を含んでいても良い。従って、天然に通常見いだされるもの以外のプリン及びピリミジンを使用していても良い。同様に本発明の本質的な意図が実行される限り、ヌクレオチドサプユニットのフラノシル部分を修飾することもできる。このような修飾の例は、2, -O-アルキルー、及び2, -N-Dの修飾の例は、0 オチドである。本発明において有用な幾つかの糖部分の2, 位の修飾の例は、0 H、SH、SCH3、OCH3、OCN、またはO(CH $_2$) $_1$ CH $_3$ (ここで $_1$ にから約10である)、及び同様の特性を有する他の置換基である。全てのこのような類似体は、本発明の遺伝子の $_1$ のの形 $_2$ ののである。

本発明のオリゴヌクレオチドは、約3から約50ヌクレオチドを含み、約8から約30ヌクレオチドを含むことが好ましく、約12から約25ヌクレオチドを含むことがさらに好ましい。本発明のオリゴヌクレオチドは、周知の方法である固相合成法により作製することができる。このような合成のための装置は、Applied Biosystemsを含む幾つかの業者により販売されている。ホスホチオエート等の他のオリゴヌクレオチドの製造も当業者に公知の方法で作製できる。

本発明のオリゴヌクレオチドは、本発明の遺伝子から転写されるmRNAとハイブリダイズできるように設計される。与えられた遺伝子の配列に基づいてアンチセンスオリゴヌクレオチドを設計する方法は、当業者であれば容易である〔たとえば、村上および牧野:細胞工学 Vol.13 No.4 p259-266 (1994)、村上章:蛋白質核酸酵素 Vol.40 No.10 p1364-1370 (1995)、竹内恒成ら:実験医学 Vol.14 No.4 p85-95 (1996)〕。 最近の研究は、mRNAの5 領域、好ましくは翻訳開始部位を含む領域に設計されたアンチセンスオリゴヌクレオチドが、遺伝子の発現の阻害に最も効果的であることを示唆している。アンチセンスオリゴヌクレオチドの長さは、15から30ヌクレオチドが好ましく、20から25ヌクレオチドがより好ましい。ホモロジー検索で他のmRNAとの相互作用がないこと、オリゴヌクレオチド配列内で二次構造を取らないことを確認しておくことは重要である。設計したアンチセンス分子が機能したかどうかの評価は、適当な細胞を

用いて、該細胞にアンチセンスオリゴヌクレオチドを導入し、当業者には公知の 方法で、対象mRNAの量(たとえば、ノーザンプロットまたはRT-PCR法)、 あるいは対象タンパク質の量(たとえば、ウエスタンプロットまたは蛍光抗体法) を測定することにより、発現抑制の効果を確認できる。

一方、三重らせん形成(トリプル・ヘリックス技術)は、核内のDNAを標的とした、主に転写の段階での遺伝子発現制御方法である。オリゴヌクレオチドは、主に転写に関与する遺伝子領域に設計され、それにより、転写及び本発明のタンパク質の産生を抑える。これらのRNA、DNA、オリゴヌクレオチドは、公知の合成装置などを用いて製造することができる。

本発明のオリゴヌクレオチドは、標的核酸配列を含む細胞に、たとえばリン酸カルシウム法、リポフェクション法、エレクトロポレーション法、マイクロインジェクション法などの DNA トランスフェクション法、またはウイルスなどの遺伝子導入ベクターの使用を含む遺伝子導入法のいずれを用いて導入してもよい。適切なレトロウイルスベクターを用いてアンチセンスオリゴヌクレオチド発現ベクターを作製し、その後、該発現ベクターを細胞とin vivoまたはex vivoで接触させることにより、標的核酸配列を含む細胞に導入できる。

本発明のDNAは、アンチセンスRNA/DNA技術またはトリプル・ヘリックス技術を用いて、本発明のタンパクを介するNF-κBの活性化を阻害するのに使用できる。

本発明のタンパク質をコードする遺伝子のアンチセンスオリゴヌクレオチドは、たとえば炎症、自己免疫疾患、感染症(たとえば、HIV感染症症)、ガンなどの、NF-κBの望ましくない活性化によって特徴つけられる疾患を治療または予防する医薬として有用である。すなわち、本発明は、上記アンチセンスオリゴヌクレオチドを有効成分として含有する医薬である。また、本発明のアンチセンスオリゴヌクレオチドは、ノーザンハイブリダイゼーション法またはPCR法を用いてそれらの疾病の検出に利用することもできる。

本発明は、NF-κBの活性化を阻害するリボザイムも含む。リボザイムは、 核酸のヌクレオチド配列を認識して、核酸を切断する活性を持つRNAである(た とえば、柳川弘志 実験医学バイオサイエンス12、RNAのニューエイジ)。リ

ボザイムは、選択された標的RNA、たとえば本発明のタンパク質をコードする mRNAを開裂するように製造することができる。本発明のタンパク質をコード するDNAのヌクレオチド配列を基に、本発明のタンパク質のmRNAを特異的 に切断するリボザイムを設計することができ、かようなリボザイムは本発明のタンパク質のmRNAに対して相補的な配列を有し、該mRNAと相補的結合し、ついで該mRNAが開裂され本発明のタンパク質の発現が減少する(または完全に発現しない)。発現減少のレベルは標的細胞内でのリボザイム発現のレベルに依存している。

よく用いられるリボザイムには、ハンマーヘッド型とヘアピン型の2種類があり、特にハンマーヘット型リボザイムは切断活性に必要な一次構造や二次構造がよく調べられており、当業者であれば、本発明のタンパク質をコードするDNAのヌクレオチド配列情報のみで容易にリボザイムの設計が可能である[たとえば、飯田ら:細胞工学 Vol. 16 No. 3, p438-445 (1997)、大川&平比良:実験医学 Vol. 12 No. 12 p83-88 (1994)]。ハンマーヘッドリボザイムは、標的RNAと相補鎖を形成する2ヶ所の認職部位(認識部位Iと認職部位II)と活性部位からなる構造をなし、標的RNAと認職部位で相補対を形成した後、標的RNAのNUXの配列(N:AまたはGまたはCまたはU、X:AまたはCまたはU)の3、末端側で切断することが知られており、特にGUC(あるいはGUA)が一番高い活性を持っことが知られており、特にGUC(あるいはGUA)が一番高い活性を持っことが知られており、特にGUC(あるいはGUA)が一番高い活性を持っことが知られており、特にGUC(あるいはGUA)が一番高い活性を持っことが知られており、特にGUC(あるいはGUA)が一番高い活性を持っことが知られており、特にGUC(あるいはGUA)が一番高い活性を持っことが知られており、特にGUC(あるいはGUA)が一番高い活性を持っことが知られており、知らにGUC(あるいはGUA)が一番高い活性を持っことが知られており、知らにGUC(あるいはGUA)が一番高い活性を持っことが知られており、第一番高い活性を持ったと、第一次には、12 No. 3, p438-445 (1997)、大川&平比良:実験医学 Vol. 12 No. 12 p83-88 (1994)、川崎&多比良:実験医学 Vol. 18 No. 3, p381-386 (2000)]。

そこでまず、本発明のDNA配列の中からGTC(またはGTA)の配列を探し出し、その前後で数ヌクレオチドから十数ヌクレオチドの相補対をつくることができるようにリボザイムを設計する。設計したリボザイムの適切性の評価は、たとえば、大川&平比良の文献〔実験医学 Vol. 12 No. 12 p83-88(1994)〕に記載の方法によって、作製したリボザイムが、イン ビトロで標的mRNAを切断できるかどうかを調べることで評価できる。リボザイムの調製は、RNA分子を合成するのための当分野で周知の方法により調製する。

別法としては、リボザイムの配列をDNA合成機で合成し、たとえばT7或いはSP6のような適切なRNAポリメラーゼプロモーターを有する多種のベクターに組み込み、イン ビトロで酵素的にRNAを合成させる方法が挙げられる。これらのリボザイムは、たとえばマイクロインジェクション法などの遺伝子導入方法によって細胞内に導入できる。あるいは別の方法として、リボザイムDNAを適当な発現ベクターに組み込んで、株細胞、細胞或いは組織内に導入する。選択された細胞中にリボザイムを導入するのに、適切なベクターを使用することができ、たとえばプラスミドベクター、動物ウイルス(たとえばレトロウイルス、アデノウイルス、ヘルペスあるいはワクシニアウイルス)ベクターがこれらの目的に通常用いられる。これらのリボザイムは、本発明のタンパク質で仲介されるNF-κ Bの活性化を阻害する作用を有する。

本発明はまた、機能を有する新規遺伝子の取得方法であり、オリゴキャッピング法を用いて完全長 c DNAライブラリーを作製する方法および該機能を有するタンパク質の存在を示すシグナル因子を用いる方法からなる取得方法に関する。シグナル因子には、たとえばレポーター遺伝子が挙げられる。

機能を有する遺伝子(cDNA)を多数取得するためには、不完全長のものが多いcDNAライブラリーを用いると効率が悪い。したがって、全体のクローンの中で、完全長のものの割合が高いライブラリーが必要となる。完全長cDNAは遺伝子から出来るmRNAの完全なコピーのことである。オリゴキャッピング法で作製したcDNAライブラリーは、完全長cDNAの割合が50~80%であり、従来の方法で作製されたcDNAライブラリーと比べて、5~10倍の完全長cDNAクローンの濃縮になっている(菅野純夫:月刊 BIO INDUSTRY Vol. 16 No. 11 p19-26)。完全長cDNAは、遺伝子の機能解析においては、タンパク質発現のために必須なクローンであり、完全長cDNAのクローンそのものが活性測定のための材料として極めて重要なものであるため、遺伝子の機能解析を試みるに際して、完全長cDNAのクローニングは必須の要件である。さらにその配列を決定することで、それがコードするタンパク質の一次配列を確定するための重要な情報となると同時に、遺伝子の全エクソンの配列も分かる。すなわち、完全長cDNAは、遺伝子を同定する上で貴重な情報、たとえばタンパク質の一次配

列、エクソンーイントロン構造、mRNAの転写開始点、プロモーターの位置などを決めるための情報をも与える。

オリゴキャッピング法による完全長 c DNAライブラリー作製は、たとえば実験医学別冊新遺伝子工学ハンドブック改訂第 3 版(1999年)に記載の方法に従い行うことができる。機能を有するタンパク質の存在を示すレポーター遺伝子は、転写因子等のタンパク質因子が結合できる適切な発現制御配列部分(1つまたは複数)と、その転写因子等による活性化を測定できる構造遺伝子部分からなる。構造遺伝子部分は、その発現産物の活性または生産量(mRNAの生産量も含まれる)を当業者が測定可能なものであれば、いかなるペプチド、タンパク質をコードする遺伝子も用いることができる。たとえば、クロラムフェニコールアセチルトランスフェラーゼ、βーガラクトシダーゼ、ルシフェラーゼ等を用いることができ、その酵素活性を測定することで利用できる。

本発明において、オリゴキャッピング法とは、鈴木・菅野 実験医学別冊 遺伝子工学ハンドブック改訂第3版に記載のように、BAP, TAP, RNAリガーゼにより、キャップ構造を合成オリゴに置換する方法である。

本発明の方法は、イン ビトロ(in vitro)の系、あるいは細胞を用いて(cell-based)の系のどちらの方法でも良く、好ましくは細胞を用いた系である。細胞は、原核大腸菌をはじめとする原核生物、酵母、真菌等の微生物、及び昆虫や動物等の細胞のいずれでも良く、好ましくは動物細胞であり、293-EBNA細胞、NIH3T3細胞が例示できる。

機能を有するタンパク質の存在を示すレポーター遺伝子としては、本願明細書に示したNF- κ B 依存レポーター遺伝子の他に、たとえば C R E B (cAMP responsive element binding protein) 結合配列あるいは A P-1 (activator protein-1)結合配列をレポーター遺伝子の発現制御配列部分に有するレポーター遺伝子が挙げられる。たとえば、C R E B を活性化する機能を有する遺伝子を取得したい場合は、C R E B 依存レポータープラスミドとオリゴキャッピング法で作製した完全長 c D N A を含む発現ベクターを細胞に共導入し、その中からレポーター活性が上昇した発現ベクターを選ぶことによって、該目的を達成することができる。また、C R E B を抑制する機能を有する遺伝子を取得したい場合は、

CREB依存レポータープラスミドとオリゴキャッピング法で作製した完全長 c DNAを含む発現ベクターを細胞に共導入し、その中からレポーター活性が減少した発現ベクターを選ぶことによって、該目的を達成することができる。この場合、細胞に何らかの刺激を加えた状態で行なっても良い。 c DNAクローン(発現ベクター)の細胞への導入は、1クローンでも良いし、複数のクローンを同時に導入しても良い。本発明の該方法の一例は、本願明細書実施例に詳細に記述してある。あるいは、完全長 c DNAを含む発現ベクターとレポーター遺伝子を細胞に導入した後、細胞を I L − 1 あるいは TNF − α などで刺激し、レポーター活性の上昇の弱いクローンを選ぶことによって、NF − κ B の活性化を抑制する機能を有する遺伝子を取得するためのスクリーニング系を構築することもできる。

しかしながら、本発明の該方法は、この方法に限定されるものではない。また、 本発明の c D N A は、完全長 c D N A であるため、その 5 ' 末端の配列がm R N Aの転写開始点であり、該 c D N A配列をゲノムのヌクレオチド配列と比較する ことにより、該遺伝子のプロモーター領域を同定することに利用できる。ゲノム のヌクレオチド配列は、データベースに公知の配列として登録されている場合は その配列を利用できる。あるいは、該cDNAを用いてたとえばハイブリダイゼ ーションによってゲノムライブラリーからクローニングし、ヌクレオチド配列を 決めることもできる。このようにして、本発明のcDNAのヌクレオチド配列を ゲノムの配列と比較することによって、その上流に存在する該遺伝子のプロモー ター領域を同定することが可能である。さらに、このようにして同定した該遺伝 子のプロモーター断片を用いて該遺伝子の発現を調べるレポータープラスミドを 作製することができる。レポータープラスミドは、大方の場合、転写開始点から その上流2kb、好ましくは転写開始点からその上流1kbのDNA断片をレポ ーター遺伝子の上流に組み込むことによって作製できる。さらに該レポータープ ラスミドは、該遺伝子の発現を増強あるいは減弱させる化合物のスクリーニング に利用できる。具体的には例えば、該レポータープラスミドで適当な細胞を形質 転換し、一定時間培養した形質転換細胞に、被験物質を任意の量添加し、一定時 間後の該細胞が発現するレポーター活性を測定し、被験物質を添加しない細胞の レポーター活性と比較することによりスクリーニングすることができる。これら

も本発明に含まれる。

また本発明は、配列番号2、4、6、8、10、12、14、16、18、2 0, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 4 4, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 6 8, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 9 2, 94, 96, 98, 100, 102, 104, 106, 108, 110, 1 12, 114, 116, 118, 120, 122, 124, 126, 128, 1 30, 132, 134, 136, 138, 140, 142, 144, 146, 1 48, 150, 151, 153, 155, 157, 159, 161, 163, 1 65、167、169、171、173、175、177または179で表され るヌクレオチド配列のうち少なくとも1以上を含むデータセットおよび/または 配列番号1、3、5、7、9、11、13、15、17、19、21、23、2 5, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 4 9, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 7 3, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 9 .7、99、101、103、105、107、109、111、113、115、 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172、174、176、178および180で表されるアミノ酸配列のうち少 なくとも1以上を含むデータセットを保存したコンピュータ読み込み可能媒体に 関する。

さらに本発明は、上記に記載の媒体上のデータと他のヌクレオチド配列のデータを比較して相同性の算出を行う方法に関する。すなわち、本発明の遺伝子およびアミノ酸配列は、その2次元および3次元構造を決定し、たとえば同様の機能を有する相同性の高いさらなる配列を同定するための貴重な情報源となる。これらの配列をコンピュータ読み込み可能媒体に保存し、ついで既知の高分子構造プログラムにおいて保存したデータを用いて、GCGのような既知検索ツールを用いてデータベースを検索すれば、データベース中の、ある相同性を有する配列を

見出すことは容易である。

コンピュータ読み取り可能媒体は情報またはデータを保存するのに用いる物体のいずれの組成物であってもよく、たとえば、市販フッロッピーディスク、テープ、チップ、ハードドライブ、コンパクトディスク、およびビデオディスク等がある。また、本媒体上のデータは、他のヌクレオチド配列のデータと比較して相同性の算出を行なう方法を可能にする。この方法には、本発明ポリヌクレオチド配列を含む第一のポリヌクレオチド配列をコンピュータ読み込み可能媒体中に提供し、次いで、該第一のポリヌクレオチド配列を少なくとも一つの第二のポリヌクレオチドまたはポリペプチド配列と比較して相同性を同定する工程を含む。

本発明はまた、配列番号 2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112、114、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、167、169、171、173、175、177または179から選択されるヌクレオチド配列の全てまたは一部を含むポリヌクレオチドが固定されている不溶性基質に関する。DNAプローブである複数の各種ポリヌクレオチドがスライドガラス等の特別に加工された基質上に固定され、次いで標識された標的ポリヌクレオチドを、固定化されたポリヌクレオチドとハイブリダイズさせ、それぞれのプローブからのシグナルを検出する。得られるデータは、解析され、遺伝子発現が測定される。

本発明はさらにまた、配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、1

11、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180で表されるアミノ酸配列から選択されるアミノ酸配列の全てまたは一部を含むポリペプチドが固定されている不溶性基質に関する。このタンパク質を固定した不溶性基質と、生物由来の細胞抽出液とを混合し、不溶性基質上に捕獲された、診断あるいは新薬開発のために有効であることが期待されるタンパク質などの細胞由来の成分を、単離あるいは同定することができる。

実施例

以下に、実施例を挙げて本発明を詳しく説明するが、本発明は、これらの例に 何ら限定されるものではない。

(実施例1)オリゴキャッピング法を用いた完全長 c D N A ライブラリーの作製

(1) ヒト肺線維芽細胞 (Cryo NHLF) からのRNA調製

ヒト肺線維芽細胞(Cryo NHLF:三光純薬株式会社より購入)を、添付のプロトコールに従って培養した。10cmシャーレ50枚まで継代培養した後、セルスクレーパーで細胞を回収した。次いで、回収した細胞からRNA抽出用試薬ISOGEN(ニッポンジーンより購入)を用いて全RNAを取得した。取得の具体的方法は、試薬のプロトコールに従った。次いで、オリゴーdT セルロース カラムを用いて、全RNAからポリA+RNAを取得した。ポリA+RNA取得の具体的方法は、上記Maniatisの実験書に従った。

(2) マウスATDC5細胞からのRNA調製

マウスEC (embryonal carcinoma) 由来クローン化細胞株ATDC5 (Atsumi, T. et al.:Cell Diff. Dev., 30:p109-116(1990)) を10 cmシャーレ50枚まで継代培養した後、上記(1)と同様の方法でポリA+RNAを取得した。ATDC5細胞の培養は、Atsumi, T. et al.:Cell Diff. Dev., 30:p109-116(1990)に記載の方法に従って培養した。

(3) オリゴキャッピング法による完全長 c D N A ライブラリー作製

上記ヒト肺線維芽細胞とATDC5細胞のポリA+RNAから、オリゴキャッピング法により完全長cDNAライブラリーをそれぞれ作製した。オリゴキャッピング法による完全長cDNAライブラリー作製の具体的方法は、菅野らの方法 [たとえば、Maruyama, K. & Sugano, S. Gene, 138:171-174(1994)、Suzuki、Y. et al. Gene、200:149-156(1997)、鈴木・菅野 実験医学別冊 遺伝子工学ハンドブック改訂第3版]に従って作製した。

(4) プラスミドDNAの調製

上記実施例で作製した完全長 c DNAライブラリーを、エレクトロポレーション法によって大腸菌TOP10株に形質転換した後、100μg/mlアンピシリンを含有するLB寒天培地に塗布し、37℃で一晩インキュベートした。続いて、アンピシリン含有LB寒天培地上で生育した大腸菌のコロニーから、QIAGEN社のQIAwell 96 Ultra Plasmid Kitを用いてプラスミドを回収した。具体的方法は、QIAwell 96 Ultra Plasmid Kitに添付のプロトコールに従った。

(実施例2) NF - κ Bを活性化する作用を有するDNAのクローニング(1) NF - κ Bを活性化する作用を有するタンパク質をコードする c DNAのスクリーニング

293-EBNA細胞(Invitrogen社より購入)を細胞培養用96 穴プレートに 1×10^4 Cells/ 100μ l/wellとなるように、5% FBS存在下のDMEM培地にまき、24時間37℃で培養した(5% CO2存在下)。次いで、FuGENE6(Roche社より購入)を用いて、pNF κ B-Luc(STRATAGENE社より購入)50ngと、上記実施例1.(4)で調製した完全長cDNA発現ベクター2 μ lを1ウエルに共導入した。導入の方法は添付のプロトコールに従った。24時間37℃で培養後、ロングタームルシフェラーゼアッセイシステム、ピッカジーンLT2.0(東洋インキ社)を用いて添付されている説明書に従い、NF $-\kappa$ Bのレポーター活性(ルシフェラーゼ活性)を測定した。なおルシフェラーゼ活性は、Perkin Elmer社

のWallac ARVOTMST 1420 MULTILABEL COU NTERを用いて行った。

(2) ヌクレオチド配列の決定

上記スクリーニングを155000クローン行い、ルシフェラーゼ活性が対照実験(完全長cDNA発現ベクターの代わりに、空ベクターpME18S-FL3を導入した細胞のルシフェラーゼ活性)と比べて5倍以上上昇しているプラスミドを選抜し、まず、クローニングされているcDNAの5'側(シークエンスプライマー:5'ーCTTCTGCTCTAAAAGCTGCG-3'(配列番号181)と3'側(シークエンスプライマー:5'ーCGACCTGCAGCTCGAGCAGCTCGAGCACA-3'(配列番号182)からそれぞれone-passシークエンスを行ない、できる限り長く決定した。なお、ヌクレオチド配列決定のための試薬や方法は、Thermo Sequenase II Dye Terminator Cycle Sequencing Kit (アマシャム ファルマシア社)、あるいはBigDye Terminator Cycle Sequencing FS Ready Reaction Kit (アプライドバイオシステムズ社)を用い、ABI PRISM 377シークエンサー、あるいは、ABI PRISM 3100シークエンサーを用い、各々キットに添付されている説明書に従って行なった。

(3) 得られたクローンのデータベース解析

得られたヌクレオチド配列について、GenBankに対するBLAST (Basic local alignment search tool) [S. F. Altschul et al., J. Mol. Biol., 215: 403-410 (1990)] 検索を行なった。その結果、148クローンが $NF-\kappa$ B を活性化する作用を有する新規のタンパク質をコードする 90 種類の遺伝子であった。

(4) 全長シークエンス

90種類の新規のクローンについて全長ヌクレオチド配列(配列番号2、4、6、8、10、12、14、16、18、20、22,24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、

80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 10 2, 104, 106, 108, 110, 112, 114, 116, 118, 12 0, 122, 124, 126, 128, 130, 132, 134, 136, 13 8, 140, 142, 144, 146, 148, 150, 151, 153, 15 5, 157, 159, 161, 163, 165, 167, 169, 171, 17 3、175、177または179)を決定し、タンパク質をコードする部分(オ ープンリーディングフレーム)のアミノ酸配列(配列番号1、3、5、7、9、 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59,61,63,65,67,69,71,73,75,77,79,81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 1 05, 107, 109, 111, 113, 115, 117, 119, 121, 1 23, 125, 127, 129, 131, 133, 135, 137, 139, 1 41, 143, 145, 147, 149, 152, 154, 156, 158, 1 60, 162, 164, 166, 168, 170, 172, 174, 176, 1 78および180)を予想した。

(実施例3) Ν F ー κ B の活性化を阻害する化合物のスクリーニング

293-EBNA細胞を細胞培養用96wellプレートに、1×10⁴Cells/100μl/wellの細胞数になるように、5%FBS存在下のDMEM培地にまき、5%CO₂存在下、37℃で24時間培養した。次いで、FuGENE6を用いて、上記実施例2で得た、配列番号5、9、17、21、35、37、41、53、57、63、67、71、75、81、87、91、93、97、121、123、129、154、158、162、168、170、172、176または178のNF-κBを活性化する作用を有するタンパク質をコードする遺伝子を含有する発現ベクター50ngと、レポータープラスミドpNFκB-Luc50ngを1wellに共導入した。1時間後、プロテアソーム阻害剤であることが知られているMG-132(CALBIOCHEMより購入)(Uehara T.et.al. J. Biol. Chem. 274 p15875-15882(1999)、Wang XC.et al.Invest.

Ophthalmol. Vis. Sci. 40 p477-486)を終濃度0. $1 \mu M$ 、0. $5 \mu M$ 、1. $0 \mu M$ 、10 μM になるようにそれぞれ培養液中に加えた。37 \mathbb{C} で24時間培養後、ピッカジーンLT2. 0を用いてレポーター活性を測定した。その結果、MG132はレポーター遺伝子の発現を抑制した(図1から図29)。

産業上の利用性

本発明により、産業上有用性の高いNF- κ Bを活性化する作用を有するタンパク質やそれらの遺伝子が提供された。本発明のタンパク質やそれらの遺伝子により、NF- κ B の過剰な活性化、又は阻害が関与する疾患の治療や予防に有用な化合物のスクリーニング、さらにそのような疾患の診断薬を作製することが可能である。更に本発明の遺伝子は、遺伝子治療に用いられる遺伝子ソースとしても有用である。

本明細書で引用した全ての刊行物、特許及び特許出願をそのまま参考として本明細書にとり入れるものとする。

請求の範囲

- 1. 以下の(a) または(b) の精製されたタンパク質。
- (a)配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかで表されるアミノ酸配列からなるタンパク質。
- (b) 配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかにおいて1若しくは複数個のアミノ酸が欠失、置換若しくは付加されたアミノ酸配列からなり、かつNF-κB(Nuclear factor kappa B)を活性化する作用を有するタンパク質。
- 2. 請求項1記載のタンパク質とその全長にわたり95%以上のアミノ酸配列の同一性を有するタンパク質であり、かつNF- κ Bを活性化する作用を有する精製されたタンパク質。

3. 以下の(a)または(b)のタンパク質をコードするヌクレオチド配列を 包含する単離されたポリヌクレオチド。

- (a) 配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかで表されるアミノ酸配列からなるタンパク質。
- (b) 配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180のいずれかにおいて1若しくは複数個のアミノ酸が欠失、置換若しくは付加されたアミノ酸配列からなり、かつNF-κBを活性化する作用を有するタンパク質。
- 4. 以下の(a)~(c)のいずれかのポリヌクレオチド配列を含む単離されたポリヌクレオチド。
- (a)配列番号2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、

48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112、114、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、167、169、171、173、175、177または179のいずれかで表されるポリヌクレオチド配列。

- (b)(a)のポリヌクレオチド配列と相補的なポリヌクレオチド配列を有するポリヌクレオチドとストリンジェントな条件下でハイブリダイズし、かつNF-κBを活性化する作用を有するタンパク質をコードするポリヌクレオチド配列。
- (c)配列番号2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112、114、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、167、169、171、173、175、177または179のいずれかにおいて、1若しくは複数個のヌクレオチドが欠失、置換若しくは付加されたポリヌクレオチド配列からなり、かつNFーκBを活性化する作用を有するタンパク質をコードするポリヌクレオチド配列。
- 5. 請求項3記載のポリヌクレオチドと全長にわたり少なくとも95%以上の同一性を有し、かつ $NF-\kappa$ Bを活性化する作用を有するタンパク質をコードするポリヌクレオチド配列を包含する単離されたポリヌクレオチド。
- 6. 請求項4記載のポリヌクレオチドと全長にわたり少なくとも95%以上の

同一性を有し、かつ $NF-\kappa B$ を活性化する作用を有するタンパク質をコードするポリヌクレオチド配列を包含する単離されたポリヌクレオチド。

- 7. 請求項3~6のいずれか1項に記載のポリヌクレオチドによりコードされる精製されたタンパク質。
- 8. 請求項3~6のいずれか1項に記載のポリヌクレオチドを含有する組換え ベクター。
- 9. 請求項8に記載の組換えベクターを含む形質転換された細胞。
- 10. 請求項1または2に記載のタンパク質が膜タンパク質である場合における、請求項9記載の細胞の膜。
- 11. (a)請求項3~6のいずれか1項に記載の単離されたポリヌクレオチドがコードするタンパク質を発現する条件下で該ポリヌクレオチドを含有する形質転換された細胞を培養し、
- (b) 培養物からタンパク質を回収する、
- ことを含むタンパク質の製造方法。
- 12. (a) 個体のゲノムにおける請求項1、2または7に記載のタンパク質をコードするヌクレオチド配列中の変異の存在または不存在を決定し、および/または
- (b) 該個体に由来するサンプル中での該タンパク質の発現量を分析する、 ことを含む、該個体における該タンパク質の発現または活性に関連した、該個体 における疾病または疾病への感受性の診断方法。
- 13. 以下の工程を含むNF-κB活性化の阻害活性または促進活性について 化合物をスクリーニングする方法。

(a) NF-κBを活性化するタンパク質をコードする遺伝子、およびNF-κBの活性化に対応した、検出可能なシグナルを提供しうる成分を細胞に提供する工程、

- (b) 該遺伝子が形質転換された細胞内で発現可能となる条件下で該形質転換された細胞を培養する工程、
- (c) 該形質転換された細胞と1あるいは複数個の候補化合物とを接触させる工程、
 - (d) 検出可能なシグナルを測定する工程、および
- (e) 該検出可能なシグナルの測定により活性化剤化合物および/または阻害剤 化合物を単離もしくは同定する工程。
- 14. 以下の工程を含む、医薬組成物を製造する方法。
- (a) NF-κBを活性化する作用を有するタンパク質をコードする遺伝子、および検出可能なシグナルを提供しうる成分を細胞に提供する工程、
- (b) 該遺伝子が形質転換された細胞内で発現可能となる条件下で該形質転換された宿主細胞を培養する工程、
- (c) 該形質転換された宿主細胞と1あるいは複数個の候補化合物とを接触させる工程、
- (d) 検出可能なシグナルを測定する工程、
- (e) 該検出可能なシグナルの測定により活性化剤化合物および/または阻害剤 化合物を単離もしくは同定する工程、および
 - (f) 単離または同定された化合物を医薬組成物として最適化する工程。
- 15. NF-κB活性化の阻害活性または促進活性について化合物をスクリー ニングするためのキットであって、
- (a) NF- κ Bを活性化するタンパク質をコードする遺伝子、およびNF- κ Bの活性化後、検出可能なシグナルを提供しうる成分により形質転換された細胞、および
 - (b) 検出可能なシグナルを測定するための試薬

を含むキット。

16. 請求項1、2または7に記載のタンパク質に特異的に結合するモノクローナルあるいはポリクローナル抗体。

- 17. 請求項1、2または7に記載のタンパク質を抗原あるいはエピトープ含有フラグメントとして非ヒト動物に投与することからなる、請求項1、2または7記載のタンパク質に特異的に結合するモノクローナルまたはポリクローナル抗体の製造方法。
- 18. NF-κBの活性化タンパク質の発現を阻害する、請求項3~6のいずれか1項に記載のポリヌクレオチドに相補的なアンチセンスオリゴヌクレオチド。
- 19. 請求項1、2または7記載のタンパク質をコードするRNAの開裂により、NF $-\kappa$ Bの活性化を阻害するリボザイム。
- 20. 炎症、自己免疫疾患、感染症、癌および骨疾患からなる群から選択される疾患の治療に有効な量の請求項13記載の方法でスクリーニングされた化合物および/または請求項16記載のモノクローナルまたはポリクローナル抗体および/または請求項18記載のアンチセンスオリゴヌクレオチドおよび/または請求項19記載のリボザイムを個体に投与することを含む疾患の治療法。
- 21. NF- κ Bの活性化を阻害または活性化するものとして請求項14に記載の方法により製造された医薬組成物。
- 22. 炎症、自己免疫疾患、癌、感染症、骨疾患、AIDS、神経変性疾患、 または虚血性障害の治療のための請求項21記載の医薬組成物。
- 23. NF-κBに関連する疾患を患っている患者に請求項14記載の方法に

より製造された医薬組成物を投与することからなる炎症、自己免疫疾患、癌、感染症、骨疾患、AIDS、神経変性疾患、または虚血性障害を治療する方法。

- 24. 請求項16記載のモノクローナルまたはポリクローナル抗体を有効成分 として含有する医薬組成物。
- 25. 請求項18記載のアンチセンスオリゴヌクレオチドを有効成分として含有する医薬組成物。
- 26. 対象疾患が炎症、自己免疫疾患、感染症、癌疾患、骨疾患、AIDS、神経変性疾患および虚血性障害からなる群から選択される、請求項24または25に記載の医薬組成物。
- 27. 機能を有する新規遺伝子の取得方法であり、少なくとも以下の工程を含む方法。
- (a) オリゴキャッピング法を用いて完全長 c D N A ライブラリーを作製し、
- (b) 完全長 c DNAおよび該機能を有するタンパク質の存在を示すシグナルを 発する因子を含有するプラスミドを細胞中にコトランスフェクションし、さらに
- (c)シグナルを発するプラスミドを選択する、

方法。

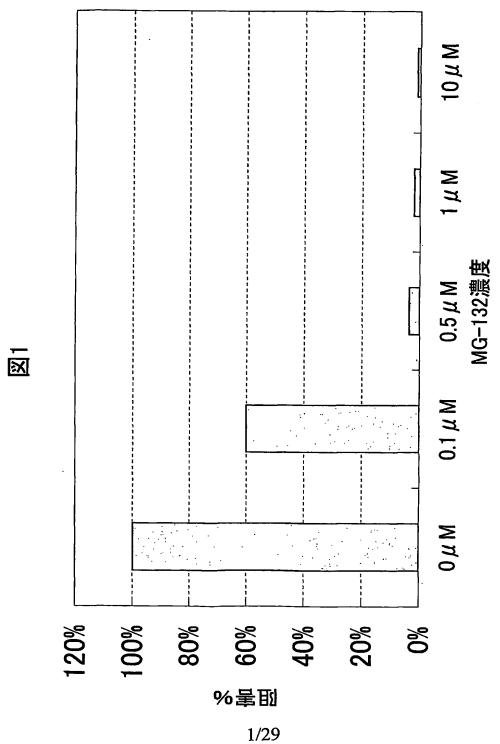
- 28. 配列番号2、4、6、8、10、12、14、16、18、20、22,
- 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46,
- 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70,
- 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94,
- 96, 98, 100, 102, 104, 106, 108, 110, 112, 11
- 4, 116, 118, 120, 122, 124, 126, 128, 130, 13
- 2, 134, 136, 138, 140, 142, 144, 146, 148, 15
- 0, 151, 153, 155, 157, 159, 161, 163, 165, 16

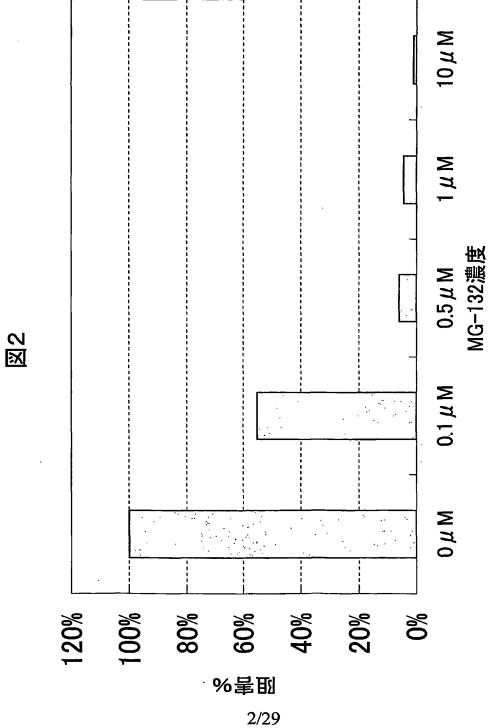
7、169、171、173、175、177または179で表されるヌクレオチド配列のうち少なくとも1以上を含むデータセットおよび/または配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178および180で表されるアミノ酸配列のうち少なくとも1以上を含むデータセットを保存したコンピュータ読み込み可能媒体。

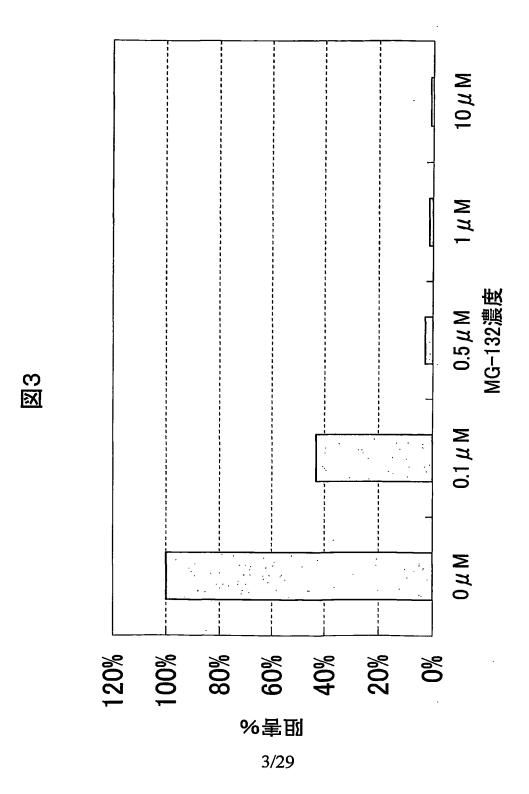
29. 請求項28に記載の媒体上のデータと他のヌクレオチド配列および/または他のアミノ酸配列のデータを比較して他のポリヌクレオチド配列および/またはアミノ酸配列との同一性の算出を行う方法。

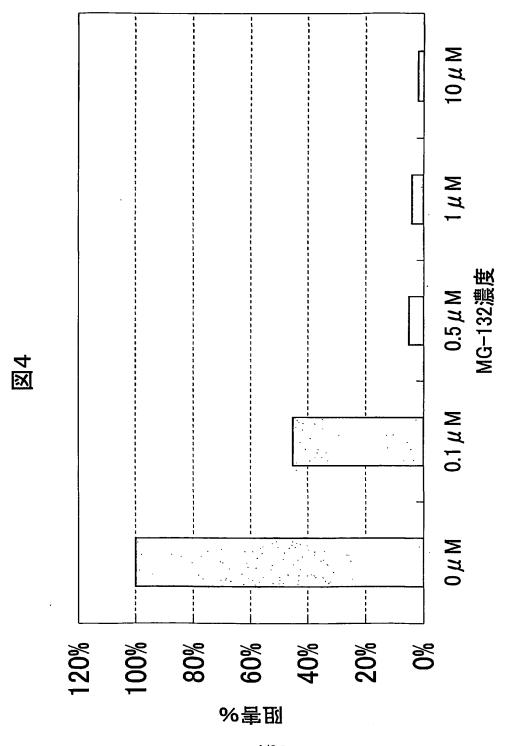
30. 配列番号2、4、6、8、10、12、14、16、18、20、22、24、26、28、30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112、114、116、118、120、122、124、126、128、130、132、134、136、138、140、142、144、146、148、150、151、153、155、157、159、161、163、165、167、169、171、173、175、177または179から選択されるヌクレオチド配列の全てまたは一部を含むポリヌクレオチドが固定されている不溶性基質。

31. 配列番号1、3、5、7、9、11、13、15、17、19、21、23、25、27、29、31、33、35、37、39、41、43、45、47、49、51、53、55、57、59、61、63、65、67、69、71、73、75、77、79、81、83、85、87、89、91、93、95、97、99、101、103、105、107、109、111、113、113、115、117、119、121、123、125、127、129、131、133、135、137、139、141、143、145、147、149、152、154、156、158、160、162、164、166、168、170、172、174、176、178または180で表されるアミノ酸配列から選択されるアミノ酸配列の全てまたは一部を含むポリペプチドが固定されている不容性基質。

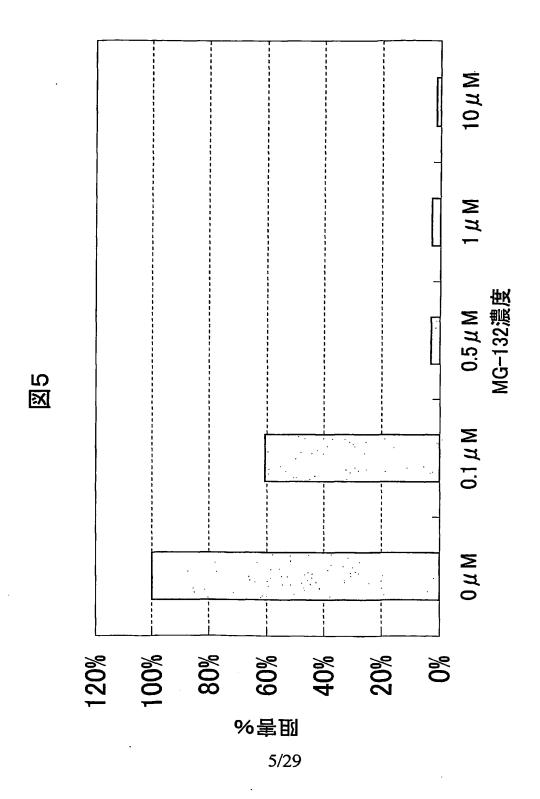


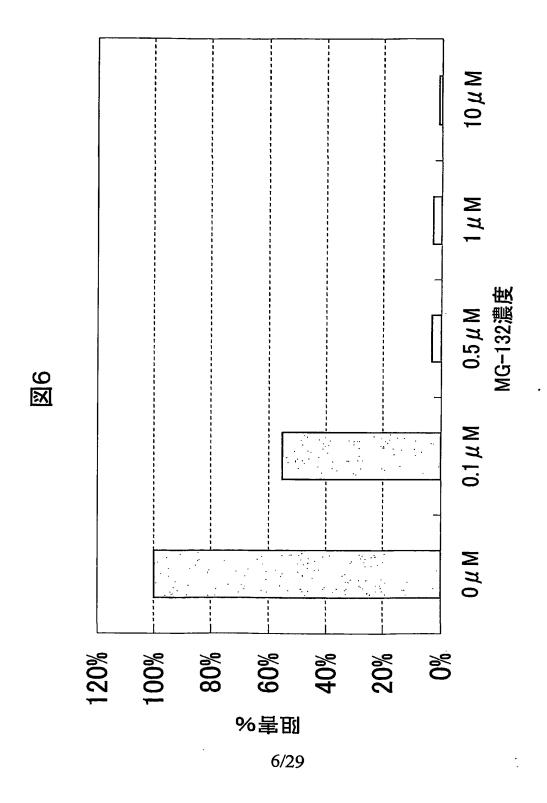


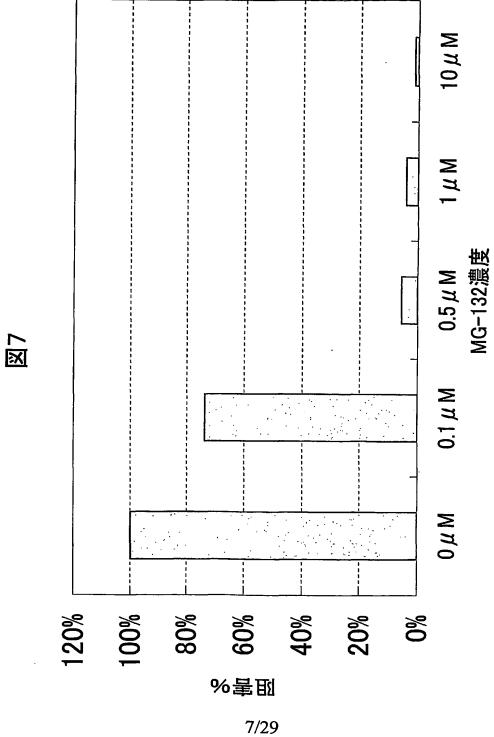


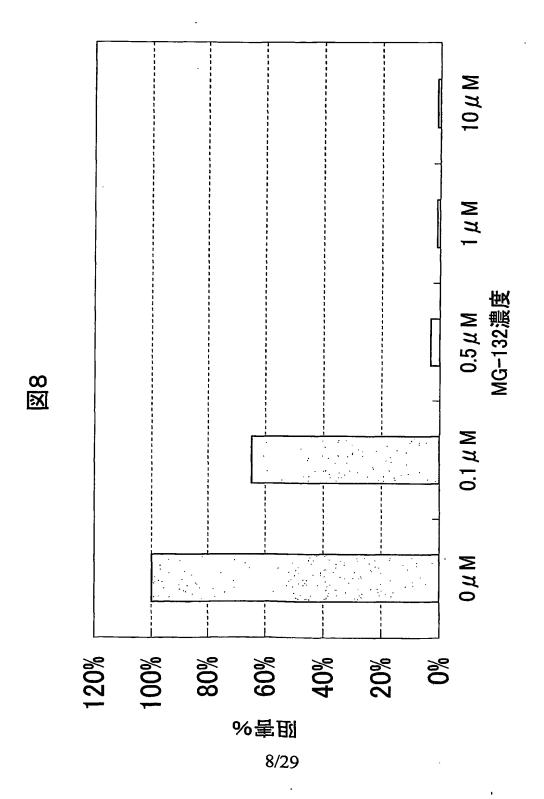


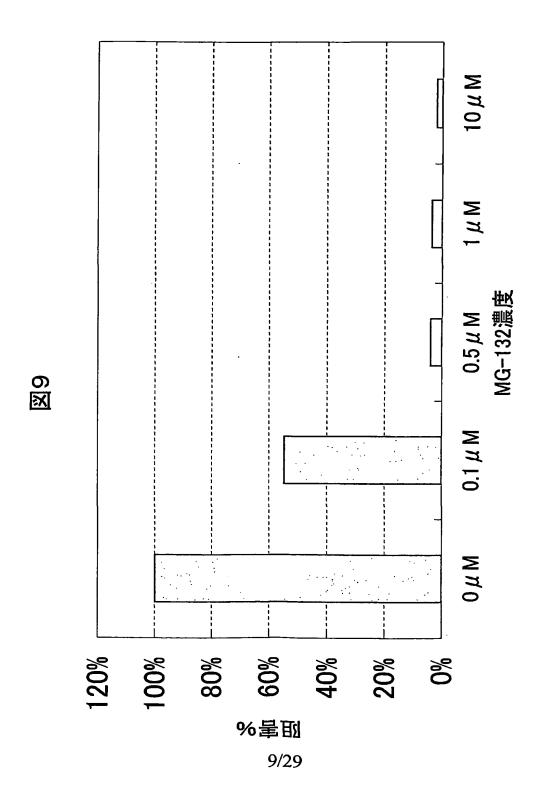
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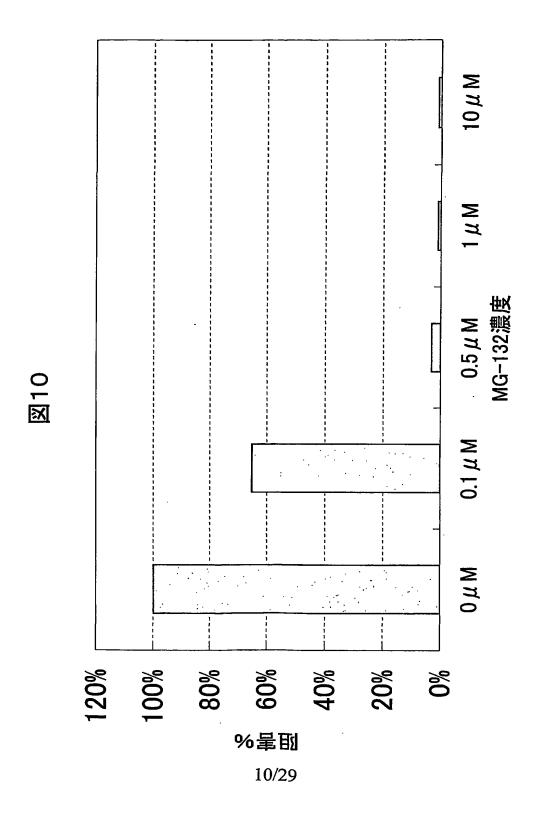


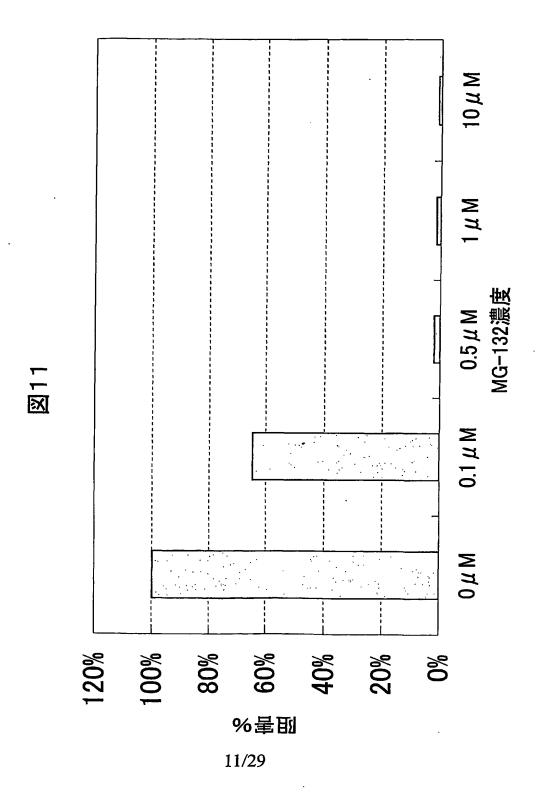


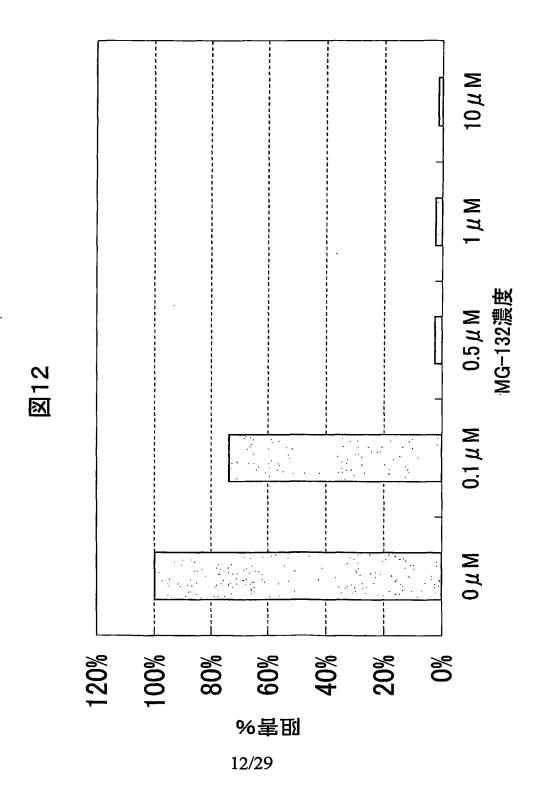


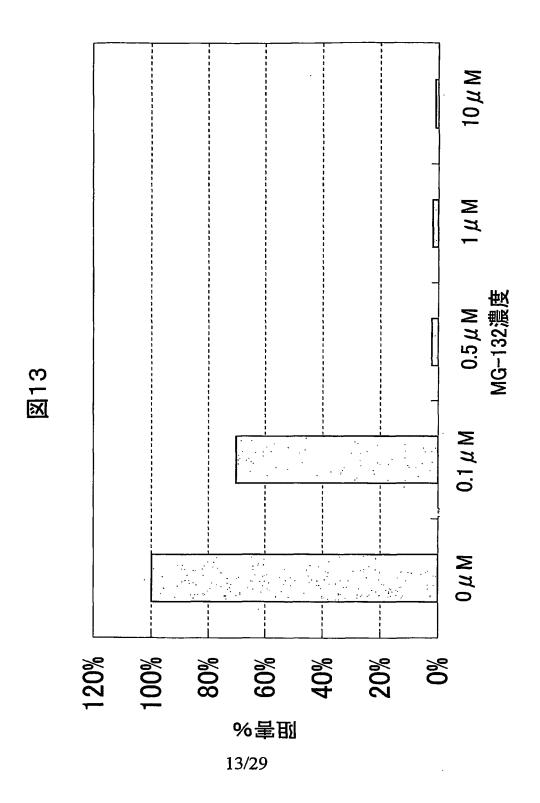


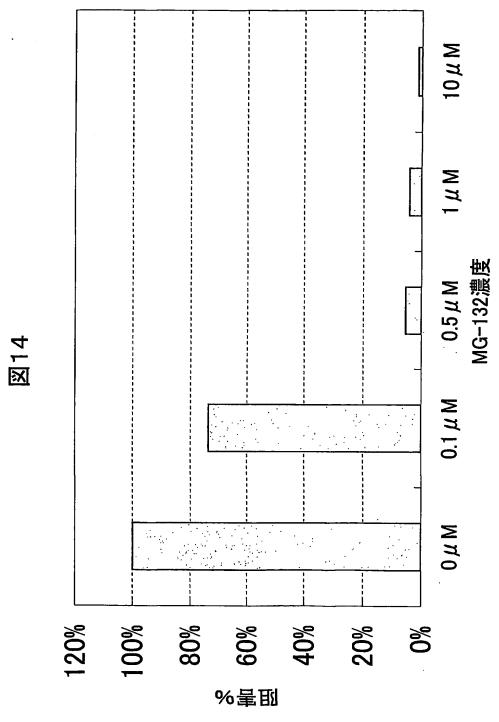




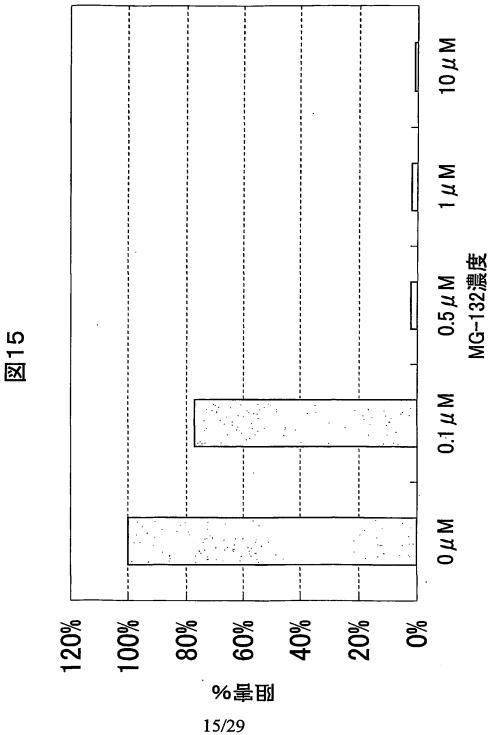


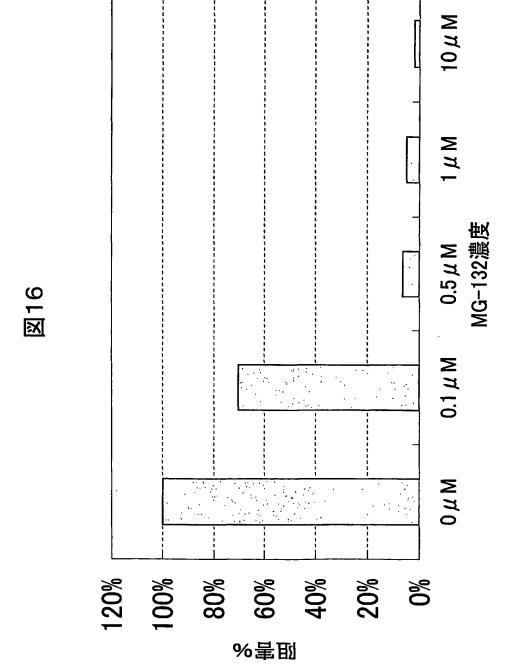




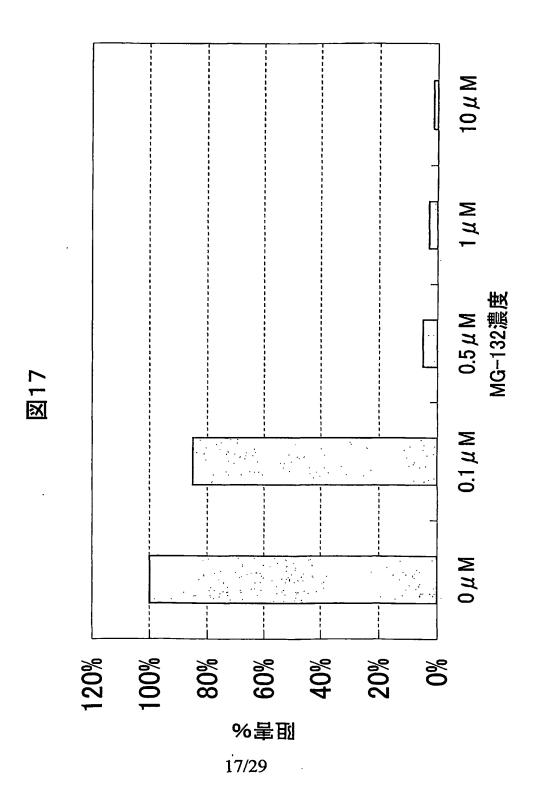


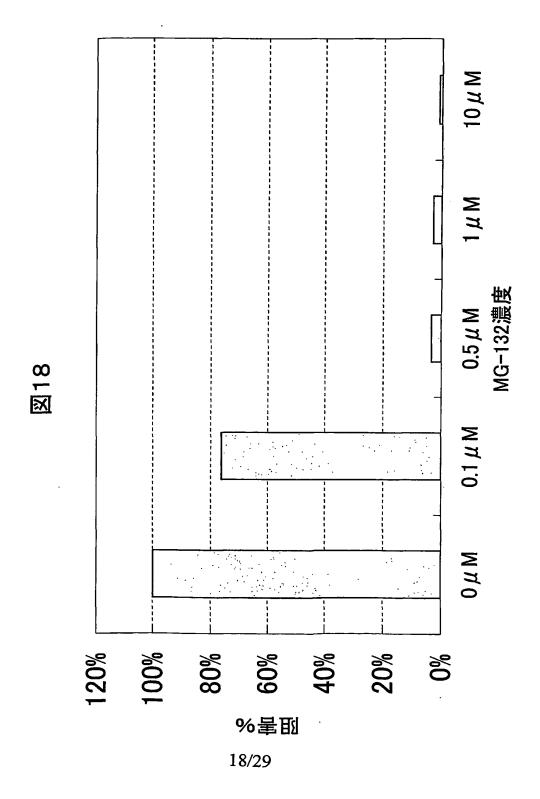
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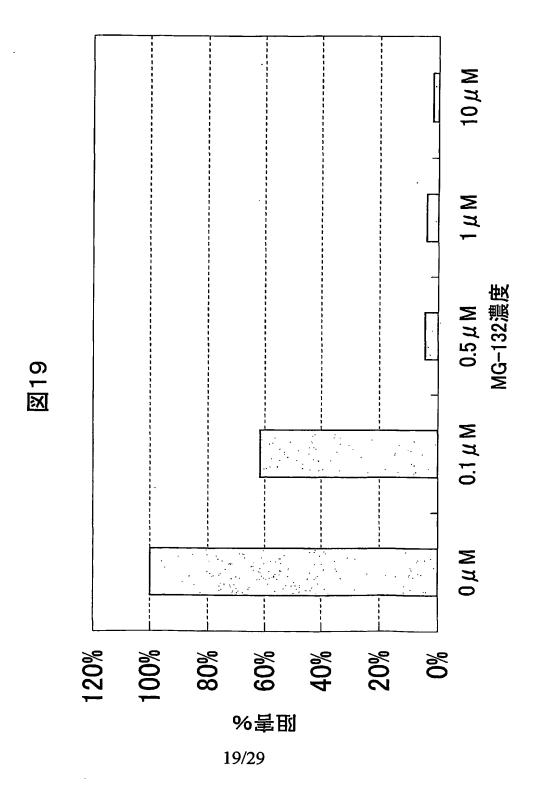


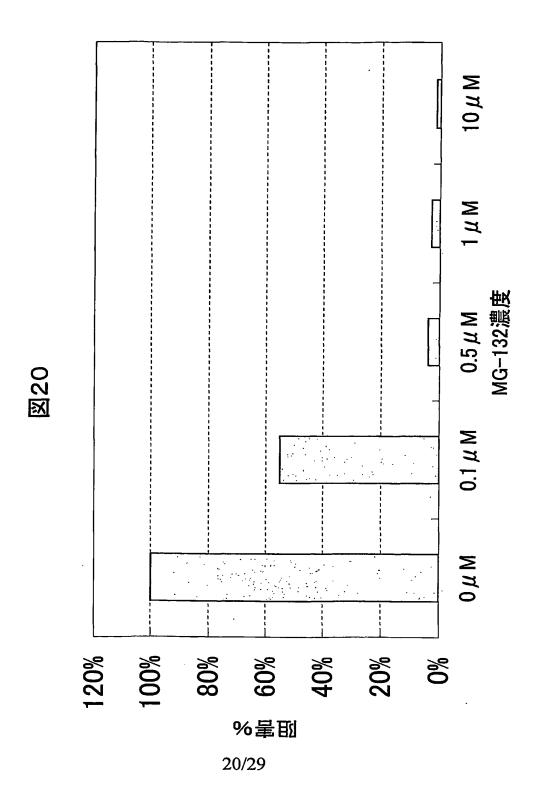


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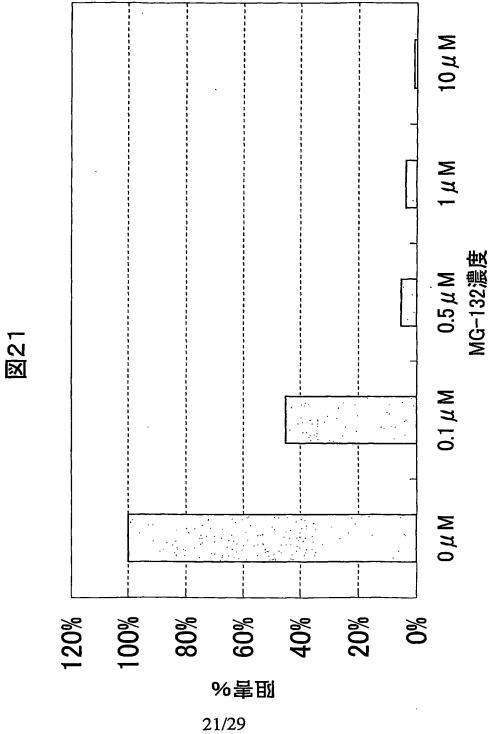


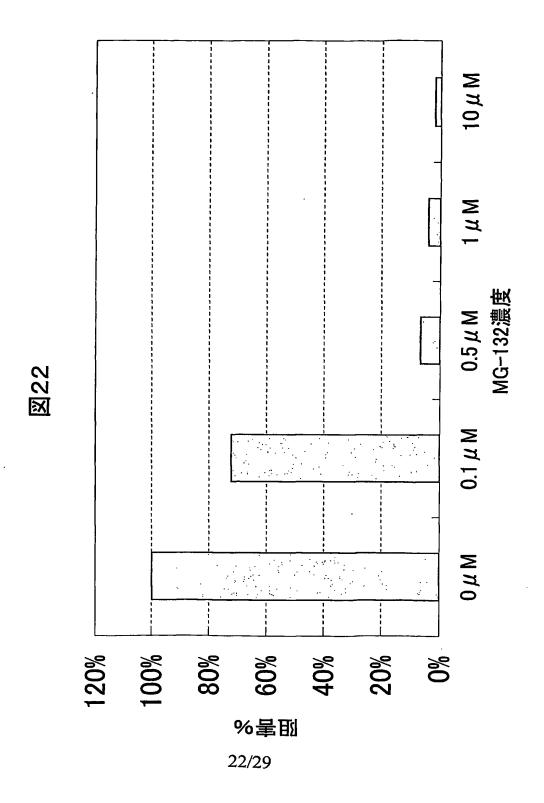


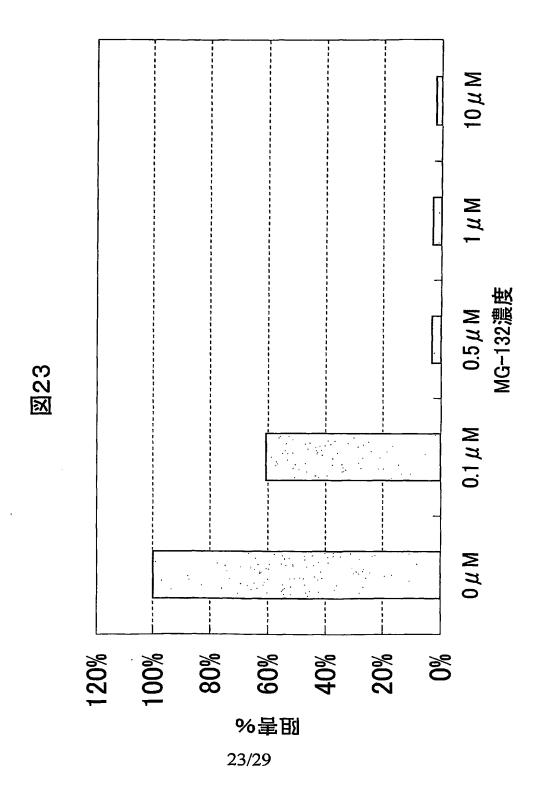


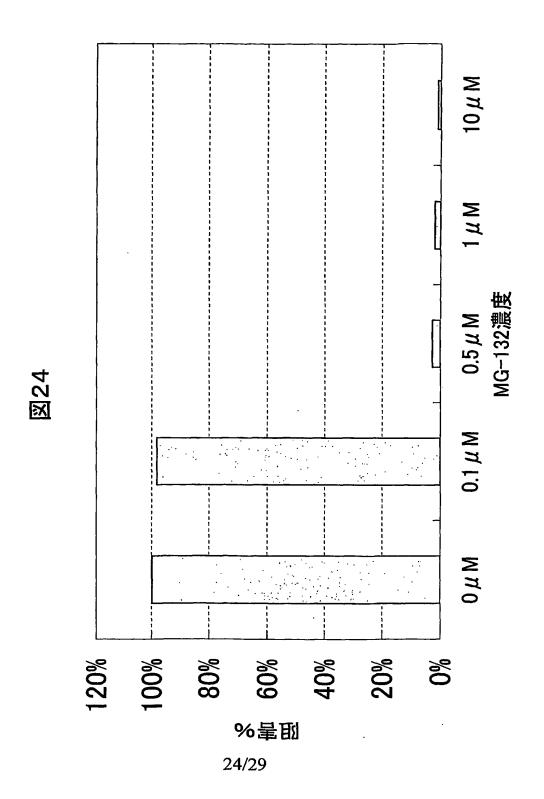


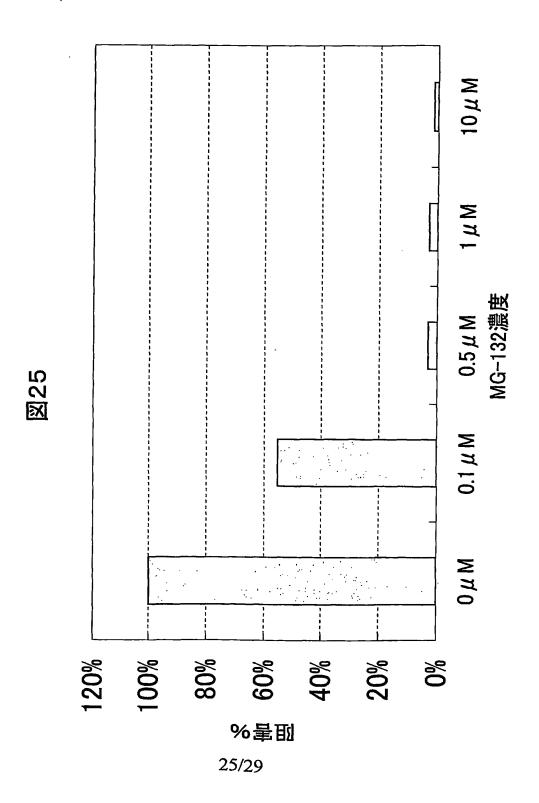
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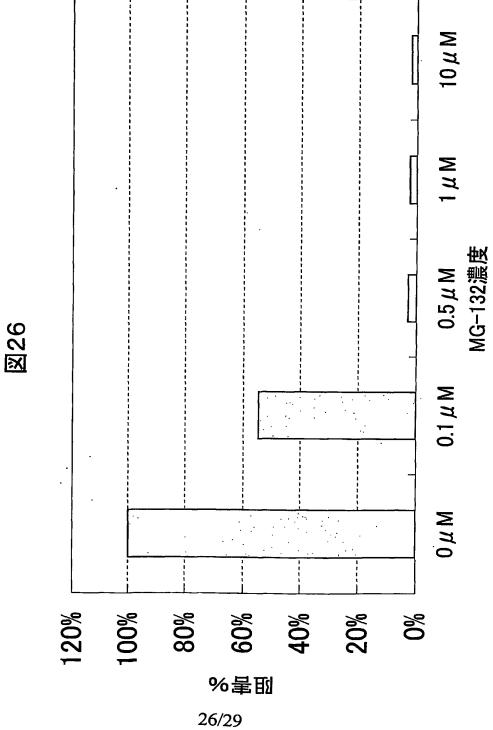


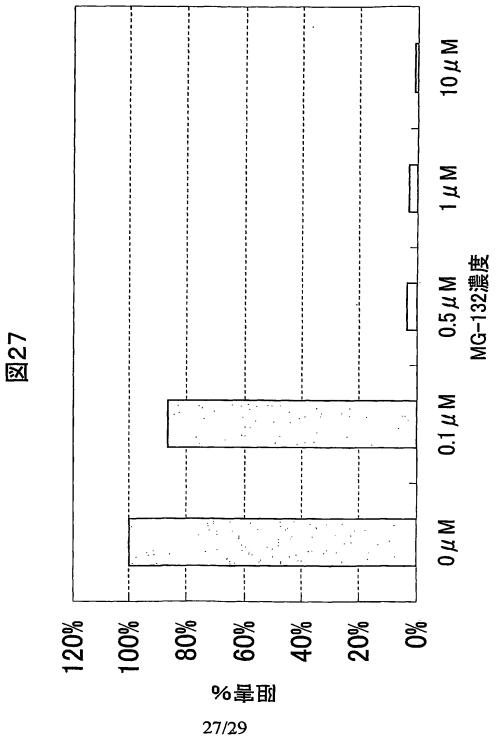


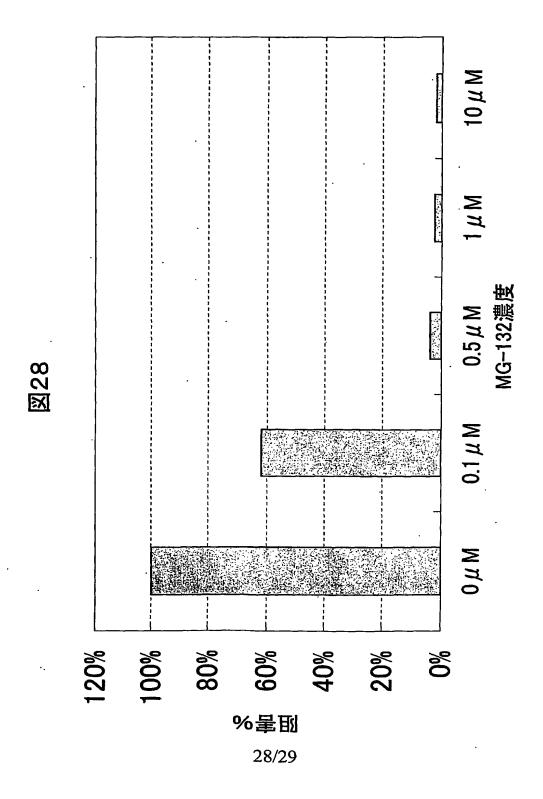


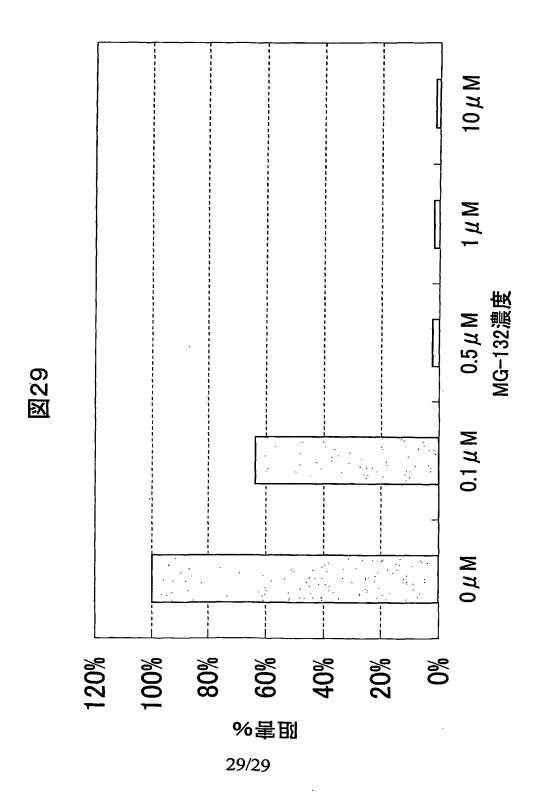












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35 40 45

Ala Gly Pro Pro Pro Pro Gly Phe Lys Ser Glu Phe Thr Gly Pro Gln

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Asn Thr Gly His Gly Ala Thr Ser Gly Phe Gly Ser Ala Phe Thr Gly

65 70 75 80

Gln Gln Gly Tyr Glu Asn Ser Gly Pro Gly Phe Trp Thr Gly Leu Gly

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Thr Gly Gly Ile Leu Gly Tyr Leu Phe Gly Ser Asn Arg Ala Ala Thr

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Pro Phe Ser Asp Ser Trp Tyr Tyr Pro Ser Tyr Pro Pro Ser Tyr Pro 2/735

115 120 125

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3/735

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Pro	Pro	Pro	Tyr	Ser	Glu	Tyr	Pro	Pro	Phe	Ser	His	Arg	Tyr	Gln	Arg	
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Phe	Thr	Asn	Ser	Ala	Gly	Pro	Pro	Pro	Pro	Gly	Phe	Lys	Ser	Glu	Phe	
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ınr	GIY	FFO	Gln		IIII	GIY	nis	GIY		IIII	Set	СТУ	LIII		Set	
				65					70					75		
gct	ttt	aca	gga	caa	caa	gga	tat	gaa	aat	tca	gga	cca	ggg	ttc	tgg	469
Ala	Phe	Thr	Gly	Gln	G1n	Gly	Tyr	Glu	Asn	Ser	Gly	Pro	Gly	Phe	Trp	
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Arg Ala Ala Thr Pro Phe Ser Asp Ser Trp Tyr Tyr Pro Ser Tyr Pro

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PCT/JP01/11389

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5/735

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35 40 45

Tyr Asp Arg Tyr Thr Thr Ser Arg Arg Leu Asp Pro Ile Pro Gln Leu
50 55 60
6/735

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Cys	Lys	Thr	Asp 100	Leu	Asp	Ile	Ala	Tyr 105	Lys	Phe	Gly	Lys	Thr 110	Val	Val
Ser	Cys	Glu 115	Gly	Tyr	Glu	Ser	Ser 120	Glu	Asp	Gln	Tyr	Val 125	Leu	Arg	Gly
Ser	Cys 130	Gly	Leu	G1u	Tyr	Asn 135	Leu	Asp	Tyr	Thr	G1u 140	Leu	Gly	Leu	Gln
Lys 145	Leu	Lys	Glu	Ser	Gly 150	Lys	Gln	His	Gly	Phe 155	Ala	Ser	Phe	Ser	Asp 160
Tyr	Tyr	Tyr	Lys	Trp 165	Ser	Ser	Ala	Asp	Ser 170	Cys	Asn	Met	Ser	Gly 175	Leu
Ile	Thr	Ile	Val 180	Val	Leu	Leu	Gly	Ile 185	Ala	Phe	Val	Val	Tyr 190	Lys	Leu
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7/735

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Leu Gly Tyr Leu Phe Gly Ser Asn Arg Ala Ala Thr Pro Phe Ser Asp
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280
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25

40

30

45

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Asp Arg Tyr Thr Thr Ser Arg Arg Leu Asp Pro Ile Pro Gln Leu Lys
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9/735

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Gln	Cys	Gln	Asn	Lys	Gly	Trp	Asp	Gly	Tyr	Asp	Val	Gln	Trp	Glu	Cys	
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Lys	Thr	Asp	Leu	Asp	Ile	Ala	Tyr	Lys	Phe	Gly	Lys	Thr	Val	Val	Ser	
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Leu	Lys	Glu	Ser	Gly	Lys	Gln	His	Gly	Phe	Ala	Ser	Phe	Ser	Asp	Tyr	
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tat	tat	aag	tgg	tcc	tcg	gcg	gat	tcc	tgt	aac	atg	agt	gga	ttg	att	645
Tyr	Tyr	Lys	Trp	Ser	Ser	Ala	Asp	Ser	Cys	Asn	Met	Ser	Gly	Leu	Ile	
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10/735

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Thr	Ile	Val	Val	Leu	Leu	Gly	Ile	Ala	Phe	Val	Val	Tyr	Lys	Leu	Phe	
		180					185					190				
ctg	agt	gac	ggg	cag	tat	tct	cct	cca	ccg	tac	tct	gag	tat	cct	cca	741
Leu	Ser	Asp	Gly	G1n	Tyr	Ser	Pro	Pro	Pro	Tyr	Ser	G1u	Tyr	Pro	Pro	
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Asn	Ser	G1y	Pro	Gly	Phe	Trp	Thr	Gly	Leu	Gly	Thr	Gly	Gly	Ile	Leu	
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Gly	Tyr	Leu	Phe	Gly	Ser	Asn	Arg	Ala	Ala	Thr	Pro	Phe	Ser	Asp	Ser	
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Ala Tyr Ser Pro Leu His Gly Gly Ser Gly Ser Tyr Ser Val Cys Ser

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Asn Ser Asp Thr Lys Thr Arg Thr Ala Ser Gly Tyr Gly Gly Thr Arg
325 330 335

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Arg Arg

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Lys Cys Val Asp Ala Arg Lys Asn His His Lys Thr Lys Trp Phe Val
50 55 60
13/735

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Ile Pro Arg Glu Ile Glu Ala Asn Asp Ile Val Phe Ser Val His Ile 85 90 95

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att	ata	gaa	aac	atg	agc	acc	aag	aag	ctg	tgc	att	gtt	ggt	ggg	att	284
Ile	Ile	Glu	Asn	Met	Ser	Thr	Lys	Lys	Leu	Cys	Ile	Val	Gly	Gly	Île	
5					10					15					20	
ctg	ctc	gtg	ttc	caa	atc	atc	gcc	ttt	ctg	gtg	gga	ggc	ttg	att	gct	332
Leu	Leu	Val	Phe	Gln	Ile	Ile	Ala	Phe	Leu	Val	Gly	Gly	Leu	Ile	Ala	
				25					30					35		
cca	ggg	ccc	aca	acg	gca	gtg	tcc	tac	atg	tcg	gtg	aaa	tgt	gtg	gat	380
Pro	Gly	Pro	Thr	Thr	Ala	Val	Ser	Tyr	Met	Ser	Val	Lys	Cys	Val	Asp	
			40					45					50			
gcc	cgt	aag	aac	cat	cac	aag	aca	aaa	tgg	ttc	gtg	cct	tgg	gga	ccc	428
Ala	Arg	Lys	Asn	His	His	Lys	Thr	Lys	Trp	Phe	Val	Pro	Trp	Gly	Pro	
		55					60					65			·	
aat	cat	tgt	gac	aag	atc	cga	gac	att	gaa	gag	gca	att	cca	agg	gaa	476
Asn	His	Cys	Asp	Lys	Ile	Arg	Asp	Ile	Glu	Glu	Ala	Ile	Pro	Arg	G1u	
	70					75					80					
att	gaa	gcc	aat	gac	atc	gtg	ttt	tct	gtt	cac	att	ссс	ctc	ССС	cac	524
Ile	Glu	Ala	Asn	Asp	Ile	Val	Phe	Ser	Val	His	Ile	Pro	Leu	Pro	His	
85					90					95					100	

atg gag atg agt cct tgg ttc caa ttc atg ctg ttt atc ctg cag ctg 572

Met Glu Met Ser Pro Trp Phe Gln Phe Met Leu Phe Ile Leu Gln Leu

105 110 115

gac att gcc ttc aag cta aac caa atc agt taagtgtact ctcctctcat 625 Asp Ile Ala Phe Lys Leu Asn Asn Gln Ile Ser

120 125

ccctttcttc cctttgagca ttgccctctt tgggttcttt ttgagccaat tctaataaaa 685

gtaaaaatgg taatagt 702

<210> 7

<211> 233

<212> PRT

<213> Homo sapiens

<400> 7

Met Ala Gly Ala Ile Ile Glu Asn Met Ser Thr Lys Lys Leu Cys Ile

1 5 10 15

Val Gly Gly Ile Leu Leu Val Phe Gln Ile Ile Ala Phe Leu Val Gly
20 25 30

Gly Leu Ile Ala Pro Gly Pro Thr Thr Ala Val Ser Tyr Met Ser Val
35 40 45

Lys Cys Val Asp Ala Arg Lys Asn His His Lys Thr Lys Trp Phe Val 16/735

W	O 02/	05373	37												PCT/JP01/11389
	50					55					60				
Pro 65	Trp	Gly	Pro	Asn _.	His 70	Cys	Asp	Lys	Ile	Arg 75	Asp	Ile	Glu	G1u	Ala 80
Ile	Pro	Arg	Glu	Ile 85	Glu	Ala	Asn	Asp	Ile 90	Val	Phe	Ser	Val	His 95	Ile
Pro	Leu	Pro	His 100	Met	Glu	Met	Ser	Pro 105	Trp	Phe	Gln	Phe	Met 110	Leu	Phe
Ile	Leu	Gln 115	Leu	Asp	Ile	Ala	Phe 120	Lys	Leu	Asn	Asn	Gln 125	Ile	Arg	Glu
Asn	Ala 130	Glu	Val	Ser	Met	Asp 135	Va1	Ser	Leu	Ala	Tyr 140	Arg	Asp	Asp	Ala
Phe 145	Ala	Glu	Trp	Thr	Glu 150	Met	Ala	His	Glu	Arg 155	Val	Pro	Arg	Lys	Leu 160
Lys	Cys	Thr	Phe	Thr 165	Ser	Pro	Lys	Thr	Pro 170	Glu	His	Glu	Gly	Arg 175	Tyr

Val Val Leu Glu Glu Asp His His Asp Val Pro Thr Pro Ser Ala Ser 195 200 205

Tyr Glu Cys Asp Val Leu Pro Tyr Ala Gln His Leu His His Tyr Gly

185

190

180

Gly Lys Ser His Leu Cys Pro Trp Asp Phe His Asp Leu Tyr Gln Tyr
210 215 220

Pro Ser Gly Met Val Phe His Arg Val
225 230

<210> 8

<211> 2409

<212> DNA

<213> Homo sapiens

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<222> (225).. (923)

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cccagaaagg aggcgaggaa ggagggagtg tgtgagagga gggagcaaaa agctcaccct 180 ·

aaaacattta tttcaaggag aaaagaaaaa ggggggggcgc aaaa atg gct ggg gca 236

Met Ala Gly Ala

1

att ata gaa aac atg agc acc aag aag ctg tgc att gtt ggt ggg att 284

Ile Ile Glu Asn Met Ser Thr Lys Lys Leu Cys Ile Val Gly Gly Ile

18/735

5			•		10					15					20		
ctg	ctc	gtg	ttc	caa	atc	atc	gcc	ttt	ctg	gtg	gga	ggc	ttg	att	gct	332	
						Ile											
				25					30					35			
cca	ggg	ccc	aca	acg	gca	gtg	tcc	tac	atg	tcg	gtg	aaa	tgt	gtg	gat	380	
Pro	G1y	Pro	Thr	Thr	Ala	Val	Ser	Tyr	Met	Ser	Val	Lys	Cys	Val	Asp		
			40					45					50				
gcc	cgt	aag	aac	cat	cac	aag	aca	aaa	tgg	ttc	gtg	cct	tgg	gga	ccc	428	
Ala	Arg	Lys	Asn	His	His	Lys	Thr	Lys	Trp	Phe	Val	Pro	Trp	Gly	Pro		
		55					60					65					
aat	cat	tgt	gac	aag	atc	cga	gac	att	gaa	gag	gca	att	cca	agg	gaa	476	
Asn	His	Cys	Asp	Lys	Ile	Arg	Asp	Ile	Glu	G1u	Ala	Ile	Pro	Arg	Glu		
	70					75					80						
	_					gtg										524	
	Glu	Ala	Asn	Asp		Val	Phe	Ser	Val		Ile	Pro	Leu	Pro			
85					90					95					100		
																550	
-						ttc				_				_		572	
Met	Glu	Met	Ser		irp	Phe	GIn	Phe		Leu	Pne	TIE	Leu		Leu		
				105					110					115			
ma o	2++	acc	++0	220	cta	220	900	000	at^	202	ass	22+	ace	are a	ata	620	
						aac Asn										620	
usp	116	ura	120	2,0	Dou	11011	non	125	116	ın E	JIU	11011	130	014	141		
								100									

19/735

PCT/JP01/11389

WO 02/053737

tcc	atg	gac	gtt	tcc	ctg	gct	tac	cgt	gat	gac	gcg	ttt	gct	gag	tgg	668
Ser	Met	Asp	Val	Ser	Leu	Ala	Tyr	Arg	Asp	Asp	Ala	Phe	Ala	Glu	Trp	
		135					140					145				
act	gaa	atg	gcc	cat	gaa	aga	gta	cca	cgg	aaa	ctc	aaa	tgc	acc	ttc	716
Thr	Glu	Met	Ala	His	Glu	Arg	Val	Pro	Arg	Lys	Leu	Lys	Cys	Thr	Phe	
	150					155					160				•	
aca	tct	ссс	aag	act	cca	gag	cat	gag	ggc	cgt	tac	tat	gaa	tgt	gat	764
Thr	Ser	Pro	Lys	Thr	Pro	Glu	His	Glu	Gly	Arg	Tyr	Tyr	Glu	Cys	Asp	
165					170					175					180	
gtc	ctt	cct	tac	gcc	cag	cat	ctt	cat	cat	tat	ggt	gtg	gta	ttg	gag	812
Val	Leu	Pro	Tyr	Ala	Gln	His	Leu	His	His	Tyr	Gly	Val	Val	Leu	Glu	
				185					190					195		
															•	
gag	gat	cac	cat	gat	gtc	ccg	acc	ccc	agt	gct	tct	gga	aaa	agt	cat	860
Glu	Asp	His	His	Asp	Va1	Pro	Thr	Pro	Ser	Ala	Ser	Gly	Lys	Ser	His	
			200					205					210			
															•	
ctt	tgc	cct	tgg	gat	ttc	cat	gac	ctt	tat	caa	tat	ccc	agt	gga	atg	908
Leu	Cys	Pro	Trp	Asp	Phe	His	Asp	Leu	Tyr	Gln	Tyr	Pro	Ser	G1y	Met	
		215					220					225				
gtt	ttc	cat	cgg	gtt	tgad	ctgga	acc 1	tggat	gcte	gc te	gtttg	ggtga	a cat	ccga	acag	963
Val	Phe	His	Arg	Val												
	230															

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<212> PRT

<213> Homo sapiens

<400> 9

Met Ala Thr Leu Trp Gly Gly Leu Leu Arg Leu Gly Ser Leu Leu Ser 22/735

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Leu Ser Cys Leu Ala Leu Ser Val Leu Leu Leu Ala Gln Leu Ser Asp 20 25 30

Ala Ala Lys Asn Phe Glu Asp Val Arg Cys Lys Cys Ile Cys Pro Pro 35 40 45

Tyr Lys Glu Asn Ser Gly His Ile Tyr Asn Lys Asn Ile Ser Gln Lys
50 55 60

Asp Cys Asp Cys Leu His Val Val Glu Pro Met Pro Val Arg Gly Pro 65 70 75 80

Asp Val Glu Ala Tyr Cys Leu Arg Cys Glu Cys Lys Tyr Glu Glu Arg 85 90 95

Ser Ser Val Thr Ile Lys Val Thr Ile Ile Ile Tyr Leu Ser Ile Leu 100 105 110

Gly Leu Leu Leu Tyr Met Val Tyr Leu Thr Leu Val Glu Pro Ile
. 115 120 125

Leu Lys Arg Arg Leu Phe Gly His Ala Gln Leu Ile Gln Ser Asp Asp 130 135 140

Asp Ile Gly Asp His Gln Pro Phe Ala Asn Ala His Asp Val Leu Ala 145 150 155 160

Arg Ser Arg Ser Arg Ala Asn Val Leu Asn Lys Val Glu Tyr Ala Gln 165 170 175

Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Ser Val Phe Asp 180 185 190

Arg His Val Val Leu Ser 195

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<212> DNA

<213> Homo sapiens

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<222> (86).. (679)

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Met Ala Thr Leu Trp Gly Gly Leu Leu

1

5

cgg ctt ggc tcc ttg ctc agc ctg tcg tgc ctg gcg ctt tcc gtg ctg 160

Arg Leu Gly Ser Leu Leu Ser Leu Ser Cys Leu Ala Leu Ser Val Leu

10 15 20 25

ctg	ctg	gcg	cag	ctg	tca	gac	gcc	gcc	aag	aat	ttc	gag	gat	gtc	aga	208
Leu	Leu	Ala	Gln	Leu	Ser	Asp	Ala	Ala	Lys	Asn	Phe	Glu	Asp	Val	Arg	
				30					35					40		
tgt	aaa	tgt	atc	tgc	cct	ccc	tat	aaa	gaa	aat	tct	ggg	cat	att	tat	256
Cys	Lys	Cys	Ile	Cys	Pro	Pro	Tyr	Lys	Glu	Asn	Ser	Gly	His	Ile	Tyr	
			45					50					55			
aat	aag	aac	ata	tct	cag	aaa	gat	tgt	gat	tgc	ctt	cat	gtt	gtg	gag	304
Asn	Lys	Asn	Ile	Ser	G1n	Lys	Asp	Cys	Asp	Cys	Leu	His	Val	Val	Glu	
		60					65					70				
ccc	atg	cct	gtg	cgg	ggg	cct	gat	gta	gaa	gca	tac	tgt	cta	cgc	tgt	352
Pro	Met	Pro	Val	Arg	Gly	Pro	Asp	Val	Glu	Ala	Tyr	Cys	Leu	Arg	Cys	
	75					80					85					
gaa	tgc	aaa	tat	gaa	gaa	aga	agc	tct	gtc	aca	atc	aag	gtt	acc	att	400
Glu	Cys	Lys	Tyr	Glu	G1u	Arg	Ser	Ser	Val	Thr	Ile	Lys	Val	Thr	Ile	
90					95					100					105	
ata	att	tat	ctc	tcc	att	ttg	ggc	ctt	cta	ctt	ctg	tac	atg	gta	tat	448
Ile	Ile	Tyr	Leu	Ser	Ile	Leu	G1y	Leu	Leu	Leu	Leu	Tyr	Met	Val	Tyr	
				110					115					120		
ctt	act	ctg	gtt	gag	ccc	ata	ctg	aag	agg	cgc	ctc	ttt	gga	cat	gca	496
Leu	Thr	Leu		Glu	Pro	Ile	Leu		Arg	Arg	Leu	Phe	Gly	His	Ala	
			125					130					135			

cag ttg ata cag agt gat gat gat att ggg gat cac cag cct ttt gca 544
Gln Leu Ile Gln Ser Asp Asp Ile Gly Asp His Gln Pro Phe Ala
140 145 150

aat gca cac gat gtg cta gcc cgc tcc cgc agt cga gcc aac gtg ctg 592
Asn Ala His Asp Val Leu Ala Arg Ser Arg Ser Arg Ala Asn Val Leu
155 160 165

aac aag gta gaa tat gca cag cag cgc tgg aag ctt caa gtc caa gag 640 Asn Lys Val Glu Tyr Ala Gln Gln Arg Trp Lys Leu Gln Val Gln Glu 170 175 180 185

cag cga aag tot gto ttt gac cgg cat gtt gto cto ago taattgggaa 689

Gln Arg Lys Ser Val Phe Asp Arg His Val Val Leu Ser

190 195

ttgaattcaa ggtgactaga aagaaacagg cagacaactg gaaagaactg actgggtttt 749
gctgggtttc attttaatac cttgttgatt tcaccaactg ttgctggaag attcaaaact 809
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aataaatctg cctgtaaatt atcttgaagt cctttacctg gaacaagcac tctcttttc 989
accacatagt tttaacttga ctttcaagat aattttcagg gtttttgttg ttgttgttt 1049
ttgtttgttt gttttggtgg gagagggag ggatgcctgg gaagtggtta acaactttt 1109
26/735

tcaagtcact ttactaaaca aacttttgta aatagacett acettctatt ttegagttte 1169
atttatattt tgeagtgtag eeageeteat caaagagetg aettacteat ttgaettttg 1229
caetgaetgt attatetggg tatetgetgt gtetgeaett eatggtaaac gggatetaaa 1289
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<211> 221

<212> PRT

<213> Homo sapiens

<400> 11

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1 5 10 15

Ser Arg Tyr Gln Gln Leu Gln Asn Glu Glu Glu Ser Gly Glu Pro Glu 20 25 30

Gln Ala Ala Gly Asp Ala Pro Pro Pro Tyr Ser Ser Ile Ser Ala Glu 27/735

W	O 02/	05373	37												PCT/JP01/11389
		35					40					45			
Ser	Ala 50	Ala	Tyr	Phe	Asp	Tyr 55	Lys	Asp	Glu	Ser	Gly 60	Phe	Pro	Lys	Pro
Pro 65	Ser	Tyr	Asn	Val	Ala 70	Thr	Thr	Leu	Pro	Ser 75	Tyr	Asp	Glu	Ala	G1u 80

Arg Thr Lys Ala Glu Ala Thr Ile Pro Leu Val Pro Gly Arg Asp Glu 85 90 95

Asp Phe Val Gly Arg Asp Asp Phe Asp Asp Ala Asp Gln Leu Arg Ile 100 105 110

Gly Asn Asp Gly Ile Phe Met Leu Thr Phe Phe Met Ala Phe Leu Phe
115 120 125

Asn Trp Ile Gly Phe Phe Leu Ser Phe Cys Leu Thr Thr Ser Ala Ala 130 135 140

Gly Arg Tyr Gly Ala Ile Ser Gly Phe Gly Leu Ser Leu Ile Lys Trp 145 150 155 160

Ile Leu Ile Val Arg Phe Ser Thr Tyr Phe Pro Gly Tyr Phe Asp Gly
165 170 175

Gln Tyr Trp Leu Trp Trp Val Phe Leu Val Leu Gly Phe Leu Leu Phe
180 185 190

Leu Arg Gly Phe Ile Asn Tyr Ala Lys Val Arg Lys Met Pro Glu Thr
195 200 205

Phe Ser Asn Leu Pro Arg Thr Arg Val Leu Phe Ile Tyr 210 215 220

<210> 12

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<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (153).. (815)

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cccctcggcc tcccagcgct cccaagccgc agcggccgcg ccccttcagc tagctcgctc 120

getegetetg etteeetget geeggetgeg ee atg geg ttg geg ttg geg geg 173... Met Ala Leu Ala Ala

1

5

ctg gcg gcg gtc gag ccg gcc tgc ggc agc cgg tac cag cag ttg cag 221 Leu Ala Ala Val Glu Pro Ala Cys Gly Ser Arg Tyr Gln Gln Leu Gln

10 15 20

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Asn	Glu	Glu	Glu	Ser	Gly	Glu	Pro	Glu	Gln	Ala	Ala	Gly	Asp	Ala	Pro	
	25					30					35					
cca	cct	tac	agc	agc	att	tct	gca	gag	agc	gca	gca	tat	ttt	gac	tac	317
Pro	Pro	Tyr	Ser	Ser	Ile	Ser	Ala	Glu	Ser	Ala	Ala	Tyr	Phe	Asp	Tyr	
40					45					50					55	
aag	gat	gag	tct	ggg	ttt	cca	aag	ccc	cca	tct	tac	aat	gta	gct	aca	365
Lys	Asp	Glu	Ser	G1y	Phe	Pro	Lys	Pro	Pro	Ser	Tyr	Asn	Val	Ala	Thr	
				60					65					70		
aca	ctg	ccc	agt	tat	gat	gaa	gcg	gag	agg	acc	aag	gct	gaa	gct	act	413
Thr	Leu	Pro		Tyr	Asp	G1u	Ala		Arg	Thr	Lys	Ala		Ala	Thr	
			75					80					85			
																401
		ttg		_												461
lle	Pro	Leu	Val	Pro	Gly	Arg		Glu	Asp	Phe	Val		Arg	Asp	Asp	
		90					95					100				
								+					_44_			500
		gat														509
rne	105	Asp	АТА	ASP	GIN		AT B	116	GLY	ASII	115	GIY	116	rne	Mec	
	103					110					113				٠	
tta	act	ttt	ttc	ata	aca	+ +c	ctc	+++	aac	† a a	att	aaa	+++	ttc	cta	557
		Phe														001
120	****		1 110	11100	125	1110	Dou	1110	11011	130	110	01,	1110	1110	135	
120					100										100	
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550		-50		455		000	0,0	30/		-00		660	500	400	, , , , , , , , , , , , , , , , , , ,	200

Ser Phe Cys Leu Thr Thr Ser Ala Ala Gly Arg Tyr Gly Ala Ile Ser 140 145 150

gga ttt ggt ctc tct cta att aaa tgg atc ctg att gtc agg ttt tcc 653
Gly Phe Gly Leu Ser Leu Ile Lys Trp Ile Leu Ile Val Arg Phe Ser
155 160 165

acc tat ttc cct gga tat ttt gat ggt cag tac tgg ctc tgg tgg gtg 701

Thr Tyr Phe Pro Gly Tyr Phe Asp Gly Gln Tyr Trp Leu Trp Trp Val

170 175 180

ttc ctt gtt tta ggc ttt ctc ctg ttt ctc aga gga ttt atc aat tat 749

Phe Leu Val Leu Gly Phe Leu Leu Phe Leu Arg Gly Phe Ile Asn Tyr

185 190 195

gca aaa gtt cgg aag atg cca gaa act ttc tca aat ctc ccc agg acc 797
Ala Lys Val Arg Lys Met Pro Glu Thr Phe Ser Asn Leu Pro Arg Thr
200 205 210 215

aga gtt ctc ttt att tat taaagatgtt ttctggcaaa ggccttcctg 845
Arg Val Leu Phe Ile Tyr

220

catttatgaa ttctctctca agaagcaaga gaacacctgc aggaagtgaa tcaagatgca 905
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<211> 242

<212> PRT

<213> Homo sapiens

<400> 13

Met Asp His His Gln Pro Gly Thr Gly Arg Tyr Gln Val Leu Leu Asn

1 5 10 15

Glu Glu Asp Asn Ser Glu Ser Ser Ala IIe Glu Gln Pro Pro Thr Ser
20 25 30

Asn Pro Ala Pro Gln Ile Val Gln Ala Ala Ser Ser Ala Pro Ala Leu 35 40 45

Glu Thr Asp Ser Ser Pro Pro Pro Tyr Ser Ser Ile Thr Val Glu Val
50 55 60

Pro Thr Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr Pro Val Pro 65 70 75 80

Pro Pro Tyr Ser Val Ala Thr Ser Leu Pro Thr Tyr Asp Glu Ala Glu

85 90 95

Lys Ala Lys Ala Ala Ala Met Ala Ala Ala Ala Ala Glu Thr Ser Gln
100 105 110

Arg Ile Glu Glu Glu Cys Pro Pro Arg Asp Asp Phe Ser Asp Ala
115
120
125
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Asp Gln Leu Arg Val Gly Asn Asp Gly IIe Phe Met Leu Ala Phe Phe 130 135 140

Met Ala Phe Ile Phe Asn Trp Leu Gly Phe Cys Leu Ser Phe Cys Ile 145 150 155 160

Thr Asn Thr Ile Ala Gly Arg Tyr Gly Ala Ile Cys Gly Phe Gly Leu 165 170 175

Ser Leu Ile Lys Trp Ile Leu Ile Val Arg Phe Ser Asp Tyr Phe Thr 180 185 190

Gly Tyr Phe Asn Gly Gln Tyr Trp Leu Trp Trp Ile Phe Leu Val Leu 195 200 205

Gly Leu Leu Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg 210 215 220

Asn Met Ser Glu Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe 225 230 235 235 240

Leu Leu

<210> 14

<211> 2324

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

⟨222⟩ (13).. (738)

<400> 14

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Met Asp His His Gln Pro Gly Thr Gly Arg Tyr Gln Val

1 5 10

ctt ctt aat gaa gag gat aac tca gaa tca tcg gct ata gag cag cca 99
Leu Leu Asn Glu Glu Asp Asn Ser Glu Ser Ser Ala Ile Glu Gln Pro
15 20 25

cct act tca aac cca gca ccg cag att gtg cag gct gcg tct tca gca 147

Pro Thr Ser Asn Pro Ala Pro Gln Ile Val Gln Ala Ala Ser Ser Ala

30 35 40 45

cca gca ctt gaa act gac tct tcc cct cca cca tat agt agt att act 195
Pro Ala Leu Glu Thr Asp Ser Ser Pro Pro Pro Tyr Ser Ser Ile Thr
50 55 60

gtg gaa gta cct aca act tca gat aca gaa gtt tac ggt gag ttt tat 243
Val Glu Val Pro Thr Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr
65 70 75

ccc gtg cca cct ccc tat agc gtt gct acc tct ctt cct aca tac gat 291
Pro Val Pro Pro Pro Tyr Ser Val Ala Thr Ser Leu Pro Thr Tyr Asp
35/735

		80					85					90				
									-4-							220
			aag													339
Glu	Ala	Glu	Lys	Ala	Lys	Ala	Ala	Ala	Met	Ala	Ala	Ala	Ala	Ala	Glu	
	95					100					105					
aca	tct	caa	aga	att	cag	gag	gaa	gag	tgt	cca	cca	aga	gat	gac	ttc	387
Thr	Ser	Gln	Arg	Ile	G1n	Glu	Glu	G1u	Cys	Pro	Pro	Arg	Asp	Asp	Phe	
110					115					120					125	
agt	gat	gca	gac	cag	ctc	aga	gtg	ggg	aat	gat	ggc	att	ttc	atg	ctg	435
Ser	Asp	Ala	Asp	Gln	Leu	Arg	Val	Gly	Asn	Asp	Gly	Ile	Phe	Met	Leu	
				130					135					140		
gca	ttt	ttc	atg	gca	ttt	att	ttc	aac	tgg	ctt	gga	ttt	tgt	tta	tcc	483
Ala	Phe	Phe	Met	Ala	Phe	Ile	Phe	Asn	Trp	Leu	Gly	Phe	Cys	Leu	Ser	
			145					150					155			
ttc	tgt	atc	acc	aat	acc	ata	gct	gga	agg	tat	ggt	gct	atc	tgc	gga	531
Phe	Cys	Ile	Thr	Asn	Thr	Ile	Ala	Gly	Arg	Tyr	Gly	Ala	Ile	Cys	Gly	
		160					165					170				
ttt	ggc	ctt	tcc	ttg	atc	aaa	tgg	atc	ctt	att	gtc	agg	ttt	tct	gat	579
			Ser													
1 110	175			204		180					185		10	501	шор	
	110					100					100					
+-+	+++	ac+	псс	+++	++~	00+	~~~	000	+ c +	+ ~~	0++	+~~	+	a+-	+++	ຂາງ
			gga													627
	rne	ınr	Gly	ıyr		Asn	σιу	GIN	ıyr		Leu	ırp	ırp	TTE		
190					195					200					205	

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ctt gta ctt ggc ctg ctc ctt ttc ttc aga gga ttt gtt aat tat cta 675
Leu Val Leu Gly Leu Leu Phe Phe Arg Gly Phe Val Asn Tyr Leu
210 215 220

aaa gtc aga aac atg tct gaa agt atg gca gct gct cat aga aca agg 723 Lys Val Arg Asn Met Ser Glu Ser Met Ala Ala Ala His Arg Thr Arg 225 230 235

tat ttc ttc tta ttg tagagactgc atcaacccga cattccttc ttataccaat 778
Tyr Phe Phe Leu Leu

240

gacaaattag tgaagaaaag acggagttc gaaattgaat ggcagggtgg tttttgctta 898

caagccattt ctgttcattc tttaagtatc tatattcat ttgttttgca catatgcata 958

tgtgcccatt taagatattt gcatatactt gatagaaacc ataaagttgt agcagttaag 1018

tccagtcaca tttggttaat cagtgtttga tataattgaa agagttgagt ggataaacag 1078

tcttccagct tgtaaatgcc attagttct gacctgacat ttagtataat aaaaatgaaa 1138

ttcttaacca tgtcaaatga tttagttct ggctcttaga ctcatctggc agttctacac 1198

atgaaacatc ttttgttata tagggtgtat tgaaacctgc agtgctgatt attagaaagg 1258

atttgtcaga tttttgaaca tgatatttac attattattt aggaaaactc ttcctgtaaa 1318 taaccatgca taacttactt tctgcaatgt tttcttagaa attgtgtcca gatagctttc 1378 actaatttta aattaagtga actaaatata tatgtgtata tgtatacaca tatatataca 1438 cacacacata tatatatta gaaacgtgag tgttaaagat agaatttgtt ttaggacaaa 1498 ttttaagaaa atgtgggaat accaaatgtc ctttataaga aaaataaatt ttattttaag 1558 ggacatacta gttttaggga ttttcagatg ggaagctgca tttttaggat tgcccatctt 1618 tcaaagttaa ttttctaaat aagataattc tcatttgtgt ttgtctttta aaaggccaat 1738 aaaatatctt tcagtatcat tgtaataatt ttttagagtt taatttgtaa agcttagcaa 1798 ataaaatctt gtactatgaa tagcttcttg ctttatgact ttaggattaa cttgtaaaaa 1858 acatatcctg aactgagata tgcaaaatac tcattttcaa gttatggaaa tgtgtttgtg 1918 gcatatagga ctgtggggtc tgtgtgta gtgagagtgt gtagccacta ttataactgg 1978 aatttaattt acattcataa actactatat ttcccatctt gcaaatcatt ttatgtctca 2038 tetgttttte ettteggtta tatetttggt tttgaatace aacatttaaa atgatggtat 2098 tttatctttt aaacttaaaa attatttaat acagctatat ggaccttata aaattgattt 2158

cttatttatt attagacatt actactaaaa ggtacatcta actattcagg gacatttttc 2218

catttccaaa aaataaaatt tattatgctt tataacctct tctgtatttt ctaatttttt 2278

cattgtcttt gataaataaa acagttttgt tttgctaata tagcct

2324

<210> 15

<211> 242

<212> PRT

<213> Homo sapiens

<400> 15

Met Asp His His Gln Pro Gly Thr Gly Arg Tyr Gln Val Leu Leu Asn
1 5 10 15

Glu Glu Asp Asn Ser Glu Ser Ser Ala Ile Glu Gln Pro Pro Thr Ser
20 25 30

Asn Pro Ala Pro Gln Ile Val Gln Ala Val Ser Ser Ala Pro Ala Leu 35 40 45

Glu Thr Asp Ser Ser Pro Pro Pro Tyr Ser Ser Ile Thr Val Glu Val
50 55 60

Pro Thr Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr Pro Val Pro 65 70 75 80

Pro	Pro	Tyr	Ser	Val	Ala	Thr	Ser	Leu	Pro	Thr	Tyr	Asp	Glu	Ala	Glu
				85					90					95	
Lys	Ala	Lys	Ala	Ala	Ala	Met	Ala	Ala	Ala	Ala	Ala	Glu	Thr	Ser	Gln
			100					105					110		
Arg	Ile	G1n	Glu	Glu	Glu	Cys	Pro	Pro	Arg	Asp	Asp	Phe	Ser	Asp	Ala
		115					120					125			
Asp	Gln	Leu	Arg	Val	Gly	Asn	Asp	Gly	Ile	Phe	Met	Leu	Ala	Phe	Phe
	130					135					140				
Met	Ala	Phe	Ile	Phe	Asn	Trp	Leu	Gly	Phe	Cys	Leu	Ser	Phe	Cys	Ile
145					150					155					160
										-					

Thr Asn Thr Ile Ala Gly Arg Tyr Gly Ala Ile Cys Gly Phe Gly Leu 165 170 175

Ser Leu Ile Lys Trp Ile Leu Ile Val Arg Phe Ser Asp Tyr Phe Thr 180 185 190

Gly Tyr Phe Asn Gly Gln Tyr Trp Leu Trp Trp Ile Phe Leu Val Leu 195 200 205

Gly Leu Leu Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg 210 215 220

Asn Met Ser Glu Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe
225 230 235 240

Leu Leu

<210> 16

<211> 2324

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (13).. (738)

<400> 16

gagccgggca gg atg gat cac cac cag ccg ggg act ggg cgc tac cag gtg 51

Met Asp His His Gln Pro Gly Thr Gly Arg Tyr Gln Val

1 5 10

ctt ctt aat gaa gag gat aac tca gaa tca tcg gct ata gag cag cca 99 Leu Leu Asn Glu Glu Asp Asn Ser Glu Ser Ser Ala Ile Glu Gln Pro

15 20 25

cct act tca aac cca gca ccg cag att gtg cag gct gtg tct tca gca 147
Pro Thr Ser Asn Pro Ala Pro Gln Ile Val Gln Ala Val Ser Ser Ala
30 35 40 45

cca gca ctt gaa act gac tct tcc cct cca cca tat agt agt att act 195
Pro Ala Leu Glu Thr Asp Ser Ser Pro Pro Pro Tyr Ser Ser Ile Thr
41/735

				50					55					60		
gtg	gaa	gta	cct	aca	act	tca	gat	aca	gaa	gtt	tac	ggt	gag	ttt	tat	243
Val	Glu	Val	Pro	Thr	Thr	Ser	Asp	Thr	Glu	Val	Tyr	Gly	Glu	Phe	Tyr	
			65					70					75			
ссс	gtg	cca	cct	ссс	tat	agc	gtt	gct	acc	tct	ctt	cct	aca	tac	gat	291
Pro	Val	Pro	Pro	Pro	Tyr	Ser	Val	Ala	Thr	Ser	Leu	Pro	Thr	Tyr	Asp	
		80					85					90				
gaa	gct	gag	aag	gct	aaa	gct	gct	gca	atg	gca	gct	gca	gca	gca	gaa	339
G1u	Ala	Glu	Lys	Ala	Lys	Ala	Ala	Ala	Met	Ala	Ala	Ala	Ala	Ala	G1u	
	95					100					105					
aca	tct	caa	aga	att	cag	gag	gaa	gag	tgt	cca	cca	aga	gat	gac	ttc	387
Thr	Ser	G1n	Arg	Ile	G1n	Glu	Glu	Glu	Cys	Pro	Pro	Arg	Asp	Asp	Phe	
110					115					120					125	
agt	gat	gca	gac	cag	ctc	aga	gtg	ggg	aat	gat	ggc	att	ttc	atg	ctg	435
Ser	Asp	Ala	Asp	G1n	Leu	Arg	Val	Gly	Asn	Asp	G1y	Ile	Phe	Met	Leu	
				130					135					140		
gca	ttt	ttc	atg	gca	ttt	att	ttc	aac	tgg	ctt	gga	ttt	tgt	tta	tcc	483
					Phe											
			145					150					155			
			_ 10													
tte	tøt	atc	acc	aat	acc	ata	get	gga	agg	tat	ggt.	get	atc	tec	gga	531
					Thr											
	٠,٠							,	3	- , -	3			٠,٠		

165

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170

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160

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ttt	ggc	ctt	tcc	ttg	atc	aaa	tgg	atc	ctt	att	gtc	agg	ttt	tct	gat	579
Phe	Gly	Leu	Ser	Leu	Ile	Lys	Trp	Ile	Leu	Ile	Val	Arg	Phe	Ser	Asp	
	175					180					185					
tat	ttt	act	gga	tat	ttc	aat	gga	cag	tat	tgg	ctt	tgg	tgg	ata	ttt	627
Tyr	Phe	Thr	Gly	Tyr	Phe	Asn	Gly	Gln	Tyr	Trp	Leu	Trp	Trp	Ile	Phe	
190					195					200					205	
ctt	gta	ctt	ggc	ctg	ctc	ctt	ttc	ttc	aga	gga	ttt	gtt	aat	tat	cta	675
Leu	Val	Leu	Gly	Leu	Leu	Leu	Phe	Phe	Arg	Gly	Phe	Val	Asn	Tyr	Leu	
				210					215					220		
aaa	gtc	aga	aac	atg	tct	gaa	agt	atg	gca	gct	gct	cat	aga	aca	agg	723
Lys	Val	Arg	Asn	Met	Ser	Glu	Ser	Met	Ala	Ala	Ala	His	Arg	Thr	Arg	
			225					230					235			
tat	ttc	ttc	tta	ttg	taga	gact	gc a	tcaa	cccg	ga ca	ttcc	tttc	tta	tacc	aat	778
Tyr	Phe	Phe	Leu	Leu												
		240														

gtgaaatttc cagatcatct gtaaacctac aactttaata gaagactact aataacagaa 838

gacaaattag tgaagaaaag acggagtttc gaaattgaat ggcagggtgg tttttgctta 898

caagccattt ctgttcattc tttaagtatc tatatttcat ttgttttgca catatgcata 958

tgtgcccatt taagatattt gcatatactt gatagaaacc ataaagttgt agcagttaag 1018

tccagtcaca tttggttaat cagtgtttga tataattgaa agagttgagt ggataaacag 1078 tettecaget tgtaaatgee attgaettet gaeetgaeat ttagtataat aaaaatgaaa 1138 ttcttaacca tgtcaaatga tttagtttct ggctcttaga ctcatctggc agttctacac 1198 atgaaacatc ttttgttata tagggtgtat tgaaacctgc agtgctgatt attagaaagg 1258 atttgtcaga tttttgaaca tgatatttac attattattt aggaaaactc ttcctgtaaa 1318 taaccatgca taacttactt tctgcaatgt tttcttagaa attgtgtcca gatagctttc 1378 actaatttta aattaagtga actaaatata tatgtgtata tgtatacaca tatatataca 1438 cacacacata tatatatta gaaacgtgag tgttaaagat agaatttgtt ttaggacaaa 1498 ttttaagaaa atgtgggaat accaaatgtc ctttataaga aaaataaatt ttattttaag 1558 ggacatacta gttttaggga ttttcagatg ggaagctgca tttttaggat tgcccatctt 1618 tcaaagttaa ttttctaaat aagataattc tcatttgtgt ttgtctttta aaaggccaat 1738 aaaatatett teagtateat tgtaataatt ttttagagtt taatttgtaa agettageaa 1798 ataaaatett gtactatgaa tagettettg etttatgaet ttaggattaa ettgtaaaaa 1858 acatateetg aactgagata tgeaaaatae teatttteaa gttatggaaa tgtgtttgtg 1918 44/735

gcatatagga ctgtgggtc tgtgtgtgta gtgagagtgt gtagccacta ttataactgg 1978

aatttaattt acattcataa actactatat ttcccatctt gcaaatcatt ttatgtctca 2038

tctgttttc ctttcggtta tatctttggt tttgaatacc aacatttaaa atgatggtat 2098

tttatctttt aaacttaaaa attatttaat acagctatat ggaccttata aaattgattt 2158

cttatttatt attagacatt actactaaaa ggtacatcta actattcagg gacatttttc 2218

catttccaaa aaataaaatt tattatgctt tataacctct tctgtattt ctaatttttt 2278

cattgtcttt gataaataaa acagttttgt tttgctaata tagcct 2324

<210> 17

<211> 336

<212> PRT

<213> Homo sapiens

<400> 17

Met Ala Arg Arg Arg Ser Gln Arg Val Cys Ala Ser Gly Pro Ser Met

1 5 10 15

Leu Asn Ser Ala Arg Gly Ala Pro Glu Leu Leu Arg Gly Thr Ala Thr
20 25 30

Asn Ala Glu Val Ser Ala Ala Ala Ala Gly Ala Thr Gly Ser Glu Glu 45/735

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35 40 45

Leu Pro Pro Gly Asp Arg Gly Cys Arg Asn Gly Gly Gly Arg Gly Pro
50 55 60

Ala Ala Thr Thr Ser Ser Thr Gly Val Ala Val Gly Ala Glu His Gly 65 70 75 80

Glu Asp Ser Leu Ser Arg Lys Pro Asp Pro Glu Pro Gly Arg Met Asp

85

90

95

His His Gln Pro Gly Thr Gly Arg Tyr Gln Val Leu Leu Asn Glu Glu
100 105 110

Asp Asn Ser Glu Ser Ser Ala Ile Glu Gln Pro Pro Thr Ser Asn Pro
115 120 125

Ala Pro Gln Ile Val Gln Ala Val Ser Ser Ala Pro Ala Leu Glu Thr 130 135 140

Asp Ser Ser Pro Pro Pro Tyr Ser Ser IIe Thr Val Glu Val Pro Thr 145 150 155 160

Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr Pro Val Pro Pro Pro 165 170 175

Tyr Ser Val Ala Thr Ser Leu Pro Thr Tyr Asp Glu Ala Glu Lys Ala 180 185 190

Lys	Ala	Ala	Ala	Met	Ala	Ala	Ala	Ala	Ala	Glu	Thr	Ser	Gln	Arg	Ile
		195					200					205			

Gln Glu Glu Cys Pro Pro Arg Asp Asp Phe Ser Asp Ala Asp Gln 210 215 220

Leu Arg Val Gly Asn Asp Gly Ile Phe Met Leu Ala Phe Phe Met Ala 225 230 235 240

Phe Ile Phe Asn Trp Leu Gly Phe Cys Leu Ser Phe Cys Ile Thr Asn 245 250 255

Thr Ile Ala Gly Arg Tyr Gly Ala Ile Cys Gly Phe Gly Leu Ser Leu 260 265 270

Ile Lys Trp Ile Leu Ile Val Arg Phe Ser Asp Tyr Phe Thr Gly Tyr
275 280 285

Phe Asn Gly Gln Tyr Trp Leu Trp Trp Ile Phe Leu Val Leu Gly Leu 290 295 300

Leu Leu Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg Asn Met 305 310 315 320

Ser Glu Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe Leu Leu 325 330 335

<210> 18

<211> 2636

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (53).. (1060)

<400> 18

cttacttttc catctcctcc cacccagcta taccctccca ctggcggcgc gg atg gca 58

Met Ala

1

cgc cgg cgg agc cag cga gtc tgc gcg agc ggt ccg agc atg ctc aat 106
Arg Arg Arg Ser Gln Arg Val Cys Ala Ser Gly Pro Ser Met Leu Asn
5 10 15

agc gcg cgc ggc gcc ccg gag ctt ctc cgc gga acc gcg acc aac gcg 154 Ser Ala Arg Gly Ala Pro Glu Leu Leu Arg Gly Thr Ala Thr Asn Ala

20 25 30

gag gtc tcg gcg gcc gct gcg gga gcc aca gga agt gaa gag ctt ccg 202 Glu Val Ser Ala Ala Ala Ala Gly Ala Thr Gly Ser Glu Glu Leu Pro 35 40 45 50

ccg gga gac cgc ggc tgc agg aac gga ggc gga agg ggc cct gcg gcg 250
Pro Gly Asp Arg Gly Cys Arg Asn Gly Gly Gly Arg Gly Pro Ala Ala

55 60 65

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acg	acg	tcg	tcg	acg	ggg	gtg	gcc	gtg	gga	gct	gag	cac	gga	gaa	gac	298
Thr	Thr	Ser	Ser	Thr	Gly	Val	Ala	Val	Gly	Ala	Glu	His	Gly	Glu	Asp	
			70			•		75					80			
tcc	ctc	tct	cgg	aag	ccg	gat	ccc	gag	ccg	ggc	agg	atg	gat	cac	cac	346
		Ser														
		85					90					95				
cag	ccg	ggg	act	ggg	cgc	tac	cag	gtg	ctt	ctt	aat	gaa	gag	gat	aac	394
Gln	Pro	Gly	Thr	Gly	Arg	Tyr	Gln	Val	Leu	Leu	Asn	Glu	Glu	Asp	Asn	
	100					105					110					
tca	gaa	tca	tcg	gct	ata	gag	cag	cca	cct	act	tca	aac	cca	gca	ccg	442
Ser	Glu	Ser	Ser	Ala	Ile	Glu	G1n	Pro	Pro	Thr	Ser	Asn	Pro	Ala	Pro	
115					120					125					130	
cag	att	gtg	cag	gct	gtg	tct	tca	gca	cca	gca	ctt	gaa	act	gac	tct	490
Gln	Ile	Val	Gln	Ala	Val	Ser	Ser	Ala	Pro	Ala	Leu	Glu	Thr	Asp	Ser	
				135					140					145		
tcc	cct	cca	cca	tat	agt	agt	att	act	gtg	gaa	gta	cct	aca	act	tca	538
Ser	Pro	Pro	Pro	Tyr	Ser	Ser	Ile	Thr	Val	Glu	Val	Pro	Thr	Thr	Ser	
			150					155					160			
gat	aca	gaa	gtt	tac	ggt	gag	ttt	tat	ссс	gtg	cca	cct	ccc	tat	agc	586
Asp	Thr	Glu	Val	Tyr	Gly	G1u	Phe	Tyr	Pro	Val	Pro	Pro	Pro	Tyr	Ser	
		165					170					175				
gtt	gct	acc	tct	ctt	cct	aca	tac	gat	gaa	gct	gag	aag	gct	aaa	gct	634
								49/7	735							

Val	Ala	Thr	Ser	Leu	Pro	Thr	Tyr	Asp	Glu	Ala	Glu	Lys	Ala	Lys	Ala	
	180					185					190					
gct	gca	atg	gca	gct	gca	gca	gca	gaa	aca	tct	caa	aga	att	cag	gag	682
Ala	Ala	Met	Ala	Ala	Ala	Ala	Ala	Glu	Thr	Ser	Gln	Arg	Ile	G1n	G1u	
195					200					205					210	
gaa	gag	tgt	cca	cca	aga	gat	gac	ttc	agt	gat	gca	gac	cag	ctc	aga	730
Glu	Glu	Cys	Pro	Pro	Arg	Asp	Asp	Phe	Ser	Asp	Ala	Asp	Gln	Leu	Arg	
				215					220					225		
gtg	ggg	aat	gat	ggc	att	ttc	atg	ctg	gca	ttt	ttc	atg	gca	ttt	att	778
Val	Gly	Asn	Asp	Gly	Ile	Phe	Met	Leu	Ala	Phe	Phe	Met	Ala	Phe	Ile	
			230					235					240			
ttc	aac	tgg	ctt	gga	ttt	tgt	tta	tcc	ttc	tgt	atc	acc	aat	acc	ata	826
Phe	Asn	Trp	Leu	Gly	Phe	Cys	Leu	Ser	Phe	Cys	Ile	Thr	Asn	Thr	Ile	
		245					250					255				
gct	gga	agg	tat _.	ggt	gct	atc	tgc	gga	ttt	ggc	ctt	tcc	ttg	atc	aaa	874
Ala	G1y	Arg	Tyr	Gly	Ala	Ile	Cys	Gly	Phe	Gly	Leu	Ser	Leu	Ile	Lys	
	260					265					270					
tgg	atc	ctt	att	gtc	agg	ttt	tct	gat	tat	ttt	act	gga	tat	ttc	aat	922
Trp	Ile	Leu	Ile	Val	Arg	Phe	Ser	Asp	Tyr	Phe	Thr	Gly	Tyr	Phe	Asn	
275					280					285					290	
gga	cag	tat	tgg	ctt	tgg	tgg	ata	ttt	ctt	gta	ctt	ggc	ctg	ctc	ctt	970
Gly	Gln	Tyr	Trp	Leu	Trp	Trp	Ile			Val	Leu	Gly	Leu	Leu	Leu	
								<i>30/</i>	73 <i>5</i>							

295 300 305

ttc ttc aga gga ttt gtt aat tat cta aaa gtc aga aac atg tct gaa 1018
Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg Asn Met Ser Glu
310 315 320

agt atg gca gct gct cat aga aca agg tat ttc ttc tta ttg 1060

Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe Leu Leu

325 330 335

tagagactgc atcaacccga cattcettic tiataccaat gigaaattic cagatcatct 1120
gtaaacctac aactitaata gaagactact aataacagaa gacaaattag tgaagaaaag 1180
acggagitte gaaattgaat ggcagggigg tittigetta caagccatti cigitcatic 1240
titaagtate tatatticat tigittigea cataigcata tigigeccatt taagatatti 1300
gcatatacti gatagaaacc ataaagitgi agcagitaag tecagicaca titiggitaat 1360
cagigittiga tataatigaa agagitgagi ggataaacag tettecagei tigiaaatigee 1420
attigettet gaccigacat tiagiataat aaaaatgaaa tiettaacca tigicaaatga 1480
titagittet ggetettaga etcateigge agitetacac atgaaacate titigitata 1540
taaggigitat tigaaaccige agigeigatt attagaaagg attigicaga tititigaaca 1600
tigatattiac attattatti aggaaaacte tieetgiaaa taaccatgea taacttacti 1660
51/735

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actactaaaa ggtacatcta actattcagg gacatttttc catttccaaa aaataaaatt 2560

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acagttttgt tttgct . 2636

<210> 19

<211> 336

<212> PRT

<213> Homo sapiens

<400> 19

Met Ala Arg Arg Ser Gln Arg Val Cys Ala Ser Gly Pro Ser Met

1 5 10 15

Leu Asn Ser Ala Arg Gly Ala Pro Glu Leu Leu Arg Gly Thr Ala Thr
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Asn Ala Glu Val Ser Ala Ala Ala Ala Gly Ala Thr Gly Ser Glu Glu
35 40 45

Leu Pro Pro Gly Asp Arg Gly Cys Arg Asn Gly Gly Gly Arg Gly Pro
50 55 60

Ala Ala Thr Thr Ser Ser Thr Gly Val Ala Val Gly Ala Glu His Gly
65 70 75 80

Glu Asp Ser Leu Ser Arg Lys Pro Asp Pro Glu Pro Gly Arg Met Asp 53/735

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His His Gln Pro Gly Thr Gly Arg Tyr Gln Val Leu Leu Asn Glu Glu Asp Asn Ser Glu Ser Ser Ala Ile Glu Gln Pro Pro Thr Ser Asn Pro Ala Pro Gln Ile Val Gln Ala Ala Ser Ser Ala Pro Ala Leu Glu Thr Asp Ser Ser Pro Pro Pro Tyr Ser Ser Ile Thr Val Glu Val Pro Thr Thr Ser Asp Thr Glu Val Tyr Gly Glu Phe Tyr Pro Val Pro Pro Tyr Ser Val Ala Thr Ser Leu Pro Thr Tyr Asp Glu Ala Glu Lys Ala Lys Ala Ala Ala Met Ala Ala Ala Ala Glu Thr Ser Gln Arg Ile

Gln Glu Glu Cys Pro Pro Arg Asp Asp Phe Ser Asp Ala Asp Gln 210 215 220

Leu Arg Val Gly Asn Asp Gly Ile Phe Met Leu Ala Phe Phe Met Ala 225 230 235 240

Phe Ile Phe Asn Trp Leu Gly Phe Cys Leu Ser Phe Cys Ile Thr Asn 245 250 255

Thr Ile Ala Gly Arg Tyr Gly Ala Ile Cys Gly Phe Gly Leu Ser Leu
260 265 270

Ile Lys Trp Ile Leu Ile Val Arg Phe Ser Asp Tyr Phe Thr Gly Tyr
275 280 285

Phe Asn Gly Gln Tyr Trp Leu Trp Trp Ile Phe Leu Val Leu Gly Leu
290 295 300

Leu Leu Phe Phe Arg Gly Phe Val Asn Tyr Leu Lys Val Arg Asn Met 305 310 315 320

Ser Glu Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe Leu Leu 325 330 335

<210> 20

<211> 2636

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (53).. (1060)

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Arg Arg Arg Ser Gln Arg Val Cys Ala Ser Gly Pro Ser Met Leu Asn
5 10 15

agc gcg cgc ggc gcc ccg gag ctt ctc cgc gga acc gcg acc aac gcg 154

Ser Ala Arg Gly Ala Pro Glu Leu Leu Arg Gly Thr Ala Thr Asn Ala

20 25 30

gag gtc tcg gcg gcc gct gcg gga gcc aca gga agt gaa gag ctt ccg 202 Glu Val Ser Ala Ala Ala Ala Gly Ala Thr Gly Ser Glu Glu Leu Pro 35 40 45 50

ccg gga gac cgc ggc tgc agg aac gga ggc gga agg ggc cct gcg gcg 250
Pro Gly Asp Arg Gly Cys Arg Asn Gly Gly Gly Arg Gly Pro Ala Ala
55 60 65

acg acg tcg tcg acg ggg gtg gcc gtg gga gct gag cac gga gaa gac 298

Thr Thr Ser Ser Thr Gly Val Ala Val Gly Ala Glu His Gly Glu Asp

70 75 80

tcc ctc tct cgg aag ccg gat ccc gag ccg ggc agg atg gat cac cac 346

Ser Leu Ser Arg Lys Pro Asp Pro Glu Pro Gly Arg Met Asp His His

85 90 95

cag ccg ggg act ggg cgc tac cag gtg ctt ctt aat gaa gag gat aac 394 56/735

G1n	Pro	Gly	Thr	Gly	Arg	Tyr	Gln	Val	Leu	Leu	Asn	Glu	Glu	Asp	Asn	
	100					105					110					
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Ser	Glu	Ser	Ser	Ala	Ile	Glu	Gln	Pro	Pro	Thr	Ser	Asn	Pro	Ala	Pro	
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cag	att	gtg	cag	gct	gcg	tct	tca	gca	cca	gca	ctt	gaa	act	gac	tct	490
Gln	Ile	Val	Gln	Ala	Ala	Ser	Ser	Ala	Pro	Ala	Leu	Glu	Thr	Asp	Ser	
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tcc	cct	cca	cca	tat	agt	agt	att	act	gtg	gaa	gta	cct	aca	act	tca	538
Ser	Pro	Pro	Pro	Tyr	Ser	Ser	Ile	Thr	Val	G1u	Val	Pro	Thr	Thr	Ser	
			150			-		155					160			
gat	aca	gaa	gtt	tac	ggt	gag	ttt	tat	ссс	gtg	cca	cct	ссс	tat	agc	586
Asp	Thŗ	G1u	Val	Tyr	Gly	Glu	Phe	Tyr	Pro	Val	Pro	Pro	Pro	Tyr	Ser	
		165					170					175				
gtt	gct	acc	tct	ctt	cct	aca	tac	gat	gaa	gct	gag	aag	gct	aaa	gct	634
Val	Ala	Thr	Ser	Leu	Pro	Thr	Tyr	Asp	Glu	Ala	Glu	Lys	Ala	Lys	Ala	
	180					185					190					
gct	gca	atg	gca	gct	gca	gca	gca	gaa	aca	tct	caa	aga	att	cag	gag	682
Ala	Ala	Met	Ala	Ala	Ala	Ala	Ala	Glu	Thr	Ser	Gln	Arg	Ile	G1n	Glu	
195					200					205					210	
gaa	gag	tgt	cca	cca	aga	gat	gac	ttc	agt	gat	gca	gac	cag	ctc	aga	730
Glu	Glu	Cys	Pro	Pro	Arg	Asp	Asp	Phe	Ser	Asp	Ala	Asp	Gln	Leu	Arg	
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agt atg gca gct gct cat aga aca agg tat ttc ttc tta ttg

1060

Ser Met Ala Ala Ala His Arg Thr Arg Tyr Phe Phe Leu Leu

325

330

335

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<211> 76

<212> PRT

<213> Homo sapiens

<400> 21

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10

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Lys Lys Phe Leu Glu Pro Tyr Ile Tyr Pro Leu Val Ser Pro Phe Val

20

25

30

Ser Arg Ile Trp Pro Lys Lys Ala Ile Gln Glu Ser Asn Asp Thr Asn

35

40

45

Lys Gly Lys Val Asn Phe Lys Gly Ala Asp Met Asn Gly Leu Pro Thr

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Lys Gly Pro Thr Glu Ile Cys Asp Lys Lys Asp

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<210> 22

<211> 1085

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (176).. (403)

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gcagagtcct aggcggtgcg cggcctcctg cctcctcct cctcggcggt cgcggcccgc 120

cggcctccgc ggtgcctgcc ttcgctctca ggttgaggag ctcaagcttg ggaaa atg 178

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gtg tgc att cct tgt atc gtc att cca gtt ctg ctc tgg atc tac aaa 226
Val Cys Ile Pro Cys Ile Val Ile Pro Val Leu Leu Trp Ile Tyr Lys
5 10 15

aaa ttc ctg gag cca tat ata tac cct ctg gtt tcc ccc ttc gtt agt 274

Lys Phe Leu Glu Pro Tyr Ile Tyr Pro Leu Val Ser Pro Phe Val Ser

20 25 30

cgt ata tgg cct aag aaa gca ata caa gaa tcc aat gat aca aac aaa 322
Arg Ile Trp Pro Lys Lys Ala Ile Gln Glu Ser Asn Asp Thr Asn Lys
35 40 45

ggc aaa gta aac ttt aag ggt gca gac atg aat gga tta cca aca aaa 370 Gly Lys Val Asn Phe Lys Gly Ala Asp Met Asn Gly Leu Pro Thr Lys 50 55 60 65

gga cca aca gaa atc tgt gat aaa aag aaa gac taaagaaatt ttcctaaagg 423 Gly Pro Thr Glu Ile Cys Asp Lys Lys Asp

70

75

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<210> 23

<211> 84

<212> PRT

<213> Homo sapiens

<400> 23

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Pro Glu Ile Gln Lys Pro Glu Arg Lys Ile Gln Phe Lys Glu Lys Val.

20

25

30

Leu Trp Thr Ala Ile Thr Leu Phe Ile Phe Leu Val Cys Cys Gln Ile

35

40

45

 $\hbox{Pro Leu Phe Gly Ile Met Ser Ser Asp Ser Ala Asp Pro Phe Tyr Trp} \\$

50

55

60

Met Arg Val Ile Leu Ala Ser Asn Arg Gly Thr Leu Met Glu His Ser

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70

75

80

Leu Ser Gly Leu

<210> 24

<211> 1593

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (65).. (316)

64/735

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cgc	c at	g gca	a ato	c aaa	a tti	t ct	g gaa	a gto	c ato	c aa	g cc	c tt	c tg	t gto	c atc	109
	Met	t Ala	ı Ile	e Lys	s Phe	e Lei	ı Glı	ı Val	l Ile	e Ly:	s Pro	o Ph	е Су	s Val	l Ile	
]	1			5	5				10)				15	
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Leu	Pro	G1u	Ile	Gln	Lys	Pro	Glu	Arg	Lys	Ile	Gln	Phe	Lys	Glu	Lys	
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gtg	ctg	tgg	acc	gct	atc	acc	ctc	ttt	atc	ttc	tta	gtg	tgc	tgc	cag	205
Val	Leu	Trp	Thr	Ala	Ile	Thr	Leu	Phe	Ile	Phe	Leu	Val	Cys	Cys	Gln	
			35					40					45			
att	ccc	ctg	ttt	ggg	atc	atg	tct	tca	gat	tca	gct	gac	cct	ttc	tat	253
Ile	Pro	Leu	Phe	Gly	Ile	Met	Ser	Ser	Asp	Ser	Ala	Asp	Pro	Phe	Tyr	
		50					55					60				
																001
								aac								301
Trp		Arg	Val	He	Leu		Ser	Asn	Arg	GLY		Leu	Met	Glu	His	
	65					70					75					
tet	ctc	tet	gge	ctt	tago	oga oʻl	ice (ectet	taos	a ca	appro	act o		agrag	rcaa	356
		Ser			v-56	, awa			, •⊶bE	, UE	-6606	-0 vg(-6046	,,,,,,,	550

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80

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aaggeaceag geeteaggag gageeeeata gteeegeetg eageetgtaa eeateggetg 1436

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<210> 25

<211> 179

<212> PRT

<213> Homo sapiens

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Met Ala Ile Lys Phe Leu Glu Val Ile Lys Pro Phe Cys Val Ile Leu

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Pro Glu Ile Gln Lys Pro Glu Arg Lys Ile Gln Phe Lys Glu Lys Val 20 25 30

Leu Trp Thr Ala Ile Thr Leu Phe Ile Phe Leu Val Cys Cys Gln Ile 35 40 45

Pro Leu Phe Gly Ile Met Ser Ser Asp Ser Ala Asp Pro Val His Ala 67/735

50 55 60

Val Val Tyr Ile Val Phe Met Leu Gly Ser Cys Ala Phe Phe Ser Lys
65 70 75 80

Thr Trp Ile Glu Val Ser Gly Ser Ser Ala Lys Asp Val Ala Lys Gln
85 90 95

Leu Lys Glu Gln Met Val Met Arg Gly His Arg Glu Thr Ser Met
100 105 110

Val His Glu Leu Asn Arg Tyr Ile Pro Thr Ala Ala Ala Phe Gly Gly
115 120 125

Leu Cys Ile Gly Ala Leu Ser Val Leu Ala Asp Phe Leu Gly Ala Ile 130 135 140

Gly Ser Gly Thr Gly Ile Leu Leu Ala Val Thr Ile Ile Tyr Gln Tyr 145 150 155 160

Phe Glu Ile Phe Val Lys Glu Gln Ser Glu Val Gly Ser Met Gly Ala 165 170 175

Leu Leu Phe

<210> 26

<211> 1820

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (114).. (650)

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<400> 26

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Met

1

gca atc aaa ttt ctg gaa gtc atc aag ccc ttc tgt gtc atc ctg ccg 164 Ala Ile Lys Phe Leu Glu Val Ile Lys Pro Phe Cys Val Ile Leu Pro

10 15

gaa att cag aag cca gag agg aag att cag ttt aag gag aaa gtg ctg 212 Glu Ile Gln Lys Pro Glu Arg Lys Ile Gln Phe Lys Glu Lys Val Leu

20 25 30

40

tgg acc gct atc acc ctc ttt atc ttc tta gtg tgc tgc cag att ccc 260
Trp Thr Ala Ile Thr Leu Phe Ile Phe Leu Val Cys Cys Gln Ile Pro

45

ctg ttt ggg atc atg tct tca gat tca gct gac ccg gtc cat gca gtt 308 Leu Phe Gly Ile Met Ser Ser Asp Ser Ala Asp Pro Val His Ala Val 50 55 60 65

69/735

gta	tac	ata	gtg	ttc	atg	ctg	ggc	tcc	tgt	gca	ttc	ttc	tcc	aaa	acg	356
Val	Tyr	Ile	Val	Phe	Met	Leu	Gly	Ser	Cys	Ala	Phe	Phe	Ser	Lys	Thr	
				70					75					80		
tgg	att	gag	gtc	tca	ggt	tcc	tct	gcc	aaa	gat	gtt	gca	aag	cag	ctg	404
Trp	Ile	Glu	Val	Ser	Gly	Ser	Ser	Ala	Lys	Asp	Val	Ala	Lys	Gln	Leu	
			85					90					95			
aag	gag	cag	cag	atg	gtg	atg	aga	ggc	cac	cga	gag	acc	tcc	atg	gtc	452
Lys	G1u	G1n	G1n	Met	Val	Met	Arg	Gly	His	Arg	Glu	Thr	Ser	Met	Val	
		100					105					110				
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His	G1u	Leu	Asn	Arg	Tyr	Ile	Pro	Thr	Ala	Ala	Ala	Phe	G1y	Gly	Leu	
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130					135					140					145	
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Ser	G1y	Thr	G1y	Ile	Leu	Leu	Ala	Val	Thr	Ile	Ile	Tyr	G1n	Tyr	Phe	
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Glu	Ile	Phe	Val	Lys	Glu	G1n	Ser	G1u	Val	Gly	Ser	Met	G1y	Ala	Leu	
			165					170					175			

70/735

ctc ttc tgagcccgtc tcccggacag gttgaggaag ctgctccaga agcgcctcgg 700 Leu Phe

aaggggagct ctcatcatgg cgcgtgctgc tgcggcatat ggacttttaa taatgttttt 760 gaatttegta ttettteatt eeactgtgta aagtgetaga catttteeaa tttaaaattt 820 tgctttttat cctggcactg gcaaaaagaa ctgtgaaagt gaatttattc agccgactgc 880 cagagaagtg ggaatggtat aggattgtcc ccaagtgtcc atgtaacttt tgttttaacc 940 tttgcacctt ctcagtgctg tatgcggctg cagccgtctc acctgtttcc ccacaaaggg 1000 aatttctcac tctggttgga agcacaaaca ctgaaatgtc tacgtttcat tttggcagta 1060 gggtgtgaag ctgggagcag atcatgtatt tcccggagac atgggacctt gctggcatgt 1120 ctccttcaca atcaggcgtg ggaatatctg gcttaggact gtttctctct aagacaccat 1180 tgttttccct tattttaaaa gtgattttt taaggacaga acttcttcca aaagagaggg 1240 atggetttee cagaagacae tetggagace ttgetggeag tgetageeag gaaacagagt 1300 gaccaaggga caagaaggga cttgcctaaa gccacccagc aactcagcag cagaaccaag 1360 atgggcccca ggctcctcca tatggcccag ggcttaccac cctatcacac gtggccttgt 1420 ctagacccag teetgageag gggagagget ettgagacet gatgeeetee tacccacatg 1480

gettaggaat gettggeete tggeaggeag geagetgtae eeaagetggt gggeaggggg 1600
ctggaaggea ceaggeetea ggaggageee eatagteeeg eetgeageet gtaaceateg 1660
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<210> 27

<211> 279

<212> PRT

<213> Homo sapiens

<400> 27

Met Glu Ala Val Val Asn Leu Tyr Gln Glu Val Met Lys His Ala Asp 1 5 10 15

Pro Arg Ile Gln Gly Tyr Pro Leu Met Gly Ser Pro Leu Leu Met Thr
20 25 30

Ser Ile Leu Leu Thr Tyr Val Tyr Phe Val Leu Ser Leu Gly Pro Arg

35 40 45

Ile Met Ala Asn Arg Lys Pro Phe Gln Leu Arg Gly Phe Met Ile Val 72/735

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50 55 60

Tyr Asn Phe Ser Leu Val Ala Leu Ser Leu Tyr Ile Val Tyr Glu Phe 65 70 75 80

Leu Met Ser Gly Trp Leu Ser Thr Tyr Thr Trp Arg Cys Asp Pro Val

85 90 95

Asp Tyr Ser Asn Ser Pro Glu Ala Leu Arg Met Val Arg Val Ala Trp
100 105 110

Leu Phe Leu Phe Ser Lys Phe Ile Glu Leu Met Asp Thr Val Ile Phe
115 120 125

Ile Leu Arg Lys Lys Asp Gly Gln Val Thr Phe Leu His Val Phe His
130 135 140

His Ser Val Leu Pro Trp Ser Trp Trp Trp Gly Val Lys Ile Ala Pro 145 150 155 160

Gly Gly Met Gly Ser Phe His Ala Met IIe Asn Ser Ser Val His Val
165 170 175

Ile Met Tyr Leu Tyr Tyr Gly Leu Ser Ala Phe Gly Pro Val Ala Gln 180 185 190

Pro Tyr Leu Trp Trp Lys Lys His Met Thr Ala Ile Gln Leu Ile Gln
195 200 205

Phe Val Leu Val Ser Leu His Ile Ser Gln Tyr Tyr Phe Met Ser Ser 210 215 220

Cys Asn Tyr Gln Tyr Pro Val Ile Ile His Leu Ile Trp Met Tyr Gly
225 230 235 240

Thr Ile Phe Phe Met Leu Phe Ser Asn Phe Trp Tyr His Ser Tyr Thr
245 250 255

Lys Gly Lys Arg Leu Pro Arg Ala Leu Gln Gln Asn Gly Ala Pro Gly
260 265 270

Ile Ala Lys Val Lys Ala Asn 275

<210> 28

<211> 1472

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (119).. (955)

<400> 28

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tgctccctcc gagcgctccg ccgttgcccg cctggcccct acggagtcct tagccagg 118
74/735

atg	gag	gct	gtt	gtg	aac	ttg	tac	caa	gag	gtg	atg	aag	cac	gca	gat	166
Met	Glu	Ala	Val	Val	Asn	Leu	Tyr	G1n	Glu	Val	Met	Lys	His	Ala	Asp	
1				5					10					15		
ccc	cgg	atc	cag	ggc	tac	cct	ctg	atg	ggg	tcc	ссс	ttg	cta	atg	acc	214
Pro	Arg	Ile	Gln	Gly	Tyr	Pro	Leu	Met	Gly	Ser	Pro	Leu	Leu	Met	Thr	
			20	•				25					30			
tcc	att	ctc	ctg	acc	tac	gtg	tac	ttc	gtt	ctc	tca	ctt	ggg	cct	cgc	262
Ser	Ile	Leu	Leu	Thr	Tyr	Val	Tyr	Phe	Val	Leu	Ser	Leu	Gly	Pro	Arg	
		35					40					45				
atc	atg	gct	aat	cgg	aag	ccc	ttc	cag	ctc	cgt	ggc	ttc	atg	att	gtc	310
Ile	Met	Ala	Asn	Arg	Lys	Pro	Phe	G1n	Leu	Arg	G1y	Phe	Met	Ile	Val	
	50					55					60					
tac	aac	ttc	tca	ctg	gtg	gca	ctc	tcc	ctc	tac	att	gtc	tat	gag	ttc	358
Tyr	Asn	Phe	Ser	Leu	Val	Ala	Leu	Ser	Leu	Tyr	Ile	Val	Tyr	G1u	Phe	
65					70					7 5					80	
ctg	atg	tcg	ggc	tgg	ctg	agc	acc	tat	acc	tgg	cgc	tgt	gac	cct	gtg	406
Leu	Met	Ser	G1y	Trp	Leu	Ser	Thr	Tyr	Thr	Trp	Arg	Cys	Asp	Pro	Val	
				85					90					95		
gac	tat	tcc	aac	agc	cct	gag	.gca	ctt	agg	atg	gtt	cgg	gtg	gcc	tgg	454
Asp	Tyr	Ser	Asn	Ser	Pro	Glu	Ala	Leu	Arg	Met	Val	Arg	Val	Ala	Trp	
			100					105					110			

ctc	ttc	ctc	ttc	tcc	aag	ttc	att	gag	ctg	atg	gac	aca	gtg	atc	ttt	502
Leu	Phe	Leu	Phe	Ser	Lys	Phe	Ile	Glu	Leu	Met	Asp	Thr	Val	Ile	Phe	
		115					120					125				
att	ctc	cga	aag	aaa	gac	ggg	cag	gtg	acc	ttc	cta	cat	gtc	ttc	cat	550
Ile	Leu	Arg	Lys	Lys	Asp	Gly	Gln	Val	Thr	Phe	Leu	His	Val	Phe	His	
	130					135					140					
cac	tct	gtg	ctt	ccc	tgg	agc	tgg	tgg	tgg	ggg	gta	aag	att	gcc	ccg	598
His	Ser	Val	Leu	Pro	Trp	Ser	Trp	Trp	Trp	Gly	Val	Lys	Ile	Ala	Pro	
145					150					155					160	
gga	gga	atg	ggc	tct	ttc	cat	gcc	atg	ata	aac	tct	tcc	gtg	cat	gtc	646
Gly	Gly	Met	Gly	Ser	Phe	His	Ala	Met	Ile	Asn	Ser	Ser	Val	His	Val	
				165					170					175		
ata	atg	tac	ctg	tac	tac	gga	tta	tct	gcc	ttt	ggc	cct	gtg	gca	caa	694
Ile	Met	Tyr	Leu	Tyr	Tyr	Gly	Leu	Ser	Ala	Phe	Gly	Pro	Val	Ala	Gln	
			180					185					190			
	tac															742
Pro	Tyr		Trp	Trp	Lys	Lys		Met	Thr	Ala	Ile		Leu	Ile	G1n	
		195					200					205				
	gtc															790
Phe	Val	Leu	Val	Ser	Leu		He	Ser	Gln	Tyr		Phe	Met	Ser	Ser	
	210					215					220					
																000
tgt	aac	tac	cag	tac	cca	gtc	att	att 76/1		ctc	atc	tgg	atg	tat	ggc	838

Cys Asn Tyr Gln Tyr Pro Val Ile Ile His Leu Ile Trp Met Tyr Gly
225 230 235 240

acc atc ttc ttc atg ctg ttc tcc aac ttc tgg tat cac tct tat acc 886

Thr Ile Phe Phe Met Leu Phe Ser Asn Phe Trp Tyr His Ser Tyr Thr

245 250 255

aag ggc aag cgg ctg ccc cgt gca ctt cag caa aat gga gct cca ggt 934 Lys Gly Lys Arg Leu Pro Arg Ala Leu Gln Gln Asn Gly Ala Pro Gly 260 265 270

att gcc aag gtc aag gcc aac tgagaagcat ggcctagata ggcgcccacc 985

Ile Ala Lys Val Lys Ala Asn

275

taagtgeete aggaetgeae ettagggeag tgteegteag tgeeetetee acetacacet 1045
gtgaccaagg ettatgtgt caggaetgag caggggaetg geeeteecet eeceaagget 1105
getetacagg gaccaegget ttggtteete aceeaactee eeegggeage teeagggatg 1165
tggeeteatt getgtetgee acteeagage tgggggetaa aagggetgta eagttatte 1225
eeeeteecet eettaaaact tgggagagga geaeteaggg etggeeeeae aaagggtete 1285
gtggeetttt teeteacaca gaagaggtea geaataatgt eaetgtggae eeagteteae 1345
teeteeacee eacacaetga ageagtaget tetgggeeaa aggteagggt gggegggge 1405

ctgggaatac agcctgtgga ggctgcttac tcaacttgtg tcttaattaa aagtgacaga 1465

ggaaacc 1472

<210> 29

<211> 137

<212> PRT

<213> Homo sapiens

<400> 29

Met Gly Phe Gly Ala Thr Leu Ala Val Gly Leu Thr Ile Phe Val Leu

1 5 10 15

Ser Val Val Thr Ile Ile Cys Phe Thr Cys Ser Cys Cys Leu
20 25 30

Tyr Lys Thr Cys Arg Arg Pro Arg Pro Val Val Thr Thr Thr Ser
35 40 45

Thr Thr Val Val His Ala Pro Tyr Pro Gln Pro Pro Ser Val Pro Pro 50 55 60

Ser Tyr Pro Gly Pro Ser Tyr Gln Gly Tyr His Thr Met Pro Pro Gln 65 70 75 80

Pro Gly Met Pro Ala Ala Pro Tyr Pro Met Gln Tyr Pro Pro Pro Tyr

85 90 95

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Pro Ala Gln Pro Met Gly Pro Pro Ala Tyr His Glu Thr Leu Ala Gly
100 105 110

Gly Ala Ala Ala Pro Tyr Pro Ala Ser Gln Pro Pro Tyr Asn Pro Ala 115 120 125

Tyr Met Asp Ala Pro Lys Ala Ala Leu 130 135

<210> 30

<211> 1788

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (145).. (555)

<400> 30

gtgcttcctg tggctgacgt catctggagg agatttgctt tctttttctc caaaagggga 60

ggaaattgaa actgagtggc ccacgatggg aagaggggaa agcccagggg tacaggaggc 120

ctctgggtga aggcagaggc taac atg ggg ttc gga gcg acc ttg gcc gtt 171

Met Gly Phe Gly Ala Thr Leu Ala Val

1

5

ggc ctg acc atc ttt gtg ctg tct gtc gtc act atc atc tgc ttc 219
79/735

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	Gly	Leu	Thr	Ile	Phe	Val	Leu	Ser	Val	Val	Thr	Ile	Ile	Ile	Cys	Phe	
	10					15					20					25	
			•														
	acc	tgc	tcc	tgc	tgc	tgc	ctt	tac	aag	acg	tgc	cgc	cga	cca	cgt	ccg	267
	Thr	Cys	Ser	Cys	Cys	Cys	Leu	Tyr	Lys	Thr	Cys	Arg	Arg	Pro	Arg	Pro	
					30					35					40		
	gtt	gtc	acc	acc	acc	aca	tcc	acc	act	gtg	gtg	cat	gcc	cct	tat	cct	315
												His					
				45					50					55	-		
•																	
	cag	cct	cca	agt	gtg	CCE	ccc	agc	tac	cct	gga	cca	agc	tac	cag	ggc	363
												Pro		-			
	0111		60	DCI	141	110	110	65	171	110	OLY	110	70	1 7 1	OIII	Oly	
			00					03					10				
	4			_4_											4		411
												gca					411
	Tyr		Thr	Met	Pro	Pro		Pro	Gly	Met	Pro	Ala	Ala	Pro	Tyr	Pro	
		75					80					85					
	atg	cag	tac	cca	cca	cct	tac	cca	gcc	cag	ccc	atg	ggc	cca	ccg	gcc	459
	Met	Gln	Tyr	Pro	Pro	Pro	Tyr	Pro	Ala	Gln	Pro	Met	Gly	Pro	Pro	Ala	
	90					95					100					105	
	tac	cac	gag	acc	ctg	gct	gga	gga	gca	gcc	gcg	ccc	tac	ccc	gcc	agc	507
	Tyr	His	Glu	Thr	Leu	Ala	Gly	Gly	Ala	Ala	Ala	Pro	Tyr	Pro	Ala	Ser	
					110					115					120		
	cag	cct	cct	tac	aac	ccg	gcc	tac	atg	gat	gcc	ccg	aag	gcg	gcc	ctc	555
	G1n	Pro	Pro	Tyr	Asn	Pro	Ala	Tyr	Met	Asp	Ala	Pro	Lys	Ala	Ala	Leu	
									80/	735							

125 130 135

tgagcattcc ctggcctctc tggctgccac ttggttatgt tgtgtgtgtg cgtgagtggt 615 gtgcaggcgc ggttccttac gccccatgtg tgctgtgtgt gtccaggcac ggttccttac 675 geoceatgtg tgetgtgtt gteetgeetg tatatgtgge tteetetgat getgaeaagg 735 tggggaacaa teettgecag agtgggetgg gaccagaett tgttetette etcacetgaa 795 attatgette etaaaatete aageeaaact caaagaatgg ggtggtgggg ggeaceetgt 855 gaggtggccc ctgagaggtg ggggcctctc cagggcacat ctggagttct tctccagctt 915 accetagggt gaccaagtag ggcetgteac accagggtgg cgcagettte tgtgtgatge 975 agatgtgtcc tggtttcggc agcgtagcca gctgctgctt gaggccatgg ctcgtccccg 1035 gagttggggg tacccgttgc agagccaggg acatgatgca ggcgaagctt gggatctggc 1095 caagttggac tttgatcctt tgggcagatg tcccattgct ccctggagcc tgtcatgcct 1155 gttggggatc aggcagcctc ctgatgccag aacacctcag gcagagccct actcagctgt 1215 acctgtctgc ctggactgtc ccctgtcccc gcatctcccc tgggaccagc tggagggcca 1275 catgcacaca cagcctagct gccccaggg agctctgctg cccttgctgg ccctgccctt 1335 cccacaggtg agcagggctc ctgtccacca gcacactcag ttctcttccc tgcagtgttt 1395 81/735

teattttatt ttagecaaac attitgeetg tittetgitt caaacatkat agitgatatg 1455
agactgaaac ceetgggttg tggagggaaa ttggeteaga gatggacaac etggeaactg 1515
tgagteetg etteecgaca eeageeteat ggaatatgea acaacteetg taccecagte 1575
caeggtgtte tggeageagg gacacetggg ceaatgggee atetggaeea aaggtggggt 1635
gtggggeet ggatggeage tetggeeeag acatgaatac eteggttee teeteetet 1695
attactgtt eaceagaget gtettagete aaatetgttg tgtttetgag tetaggget 1755
gtacacttgt ttataataaa tgeaategtt tgg 1788

<210> 31

<211> 118

<212> PRT

<213> Homo sapiens

<400> 31

Met Gly Phe Gly Ala Thr Leu Ala Val Gly Leu Thr Ile Phe Val Leu

1 5 10 15

Ser Val Val Thr Ile Ile Cys Phe Thr Cys Ser Cys Cys Leu
20 25 30

Tyr Lys Thr Cys Arg Arg Pro Arg Pro Val Val Thr Thr Thr Ser 82/735

35 40 45

Thr Thr Val Val His Ala Pro Tyr Pro Gln Pro Pro Ser Val Pro Pro 50 55 60

Ser Tyr Pro Gly Pro Ser Tyr Gln Gly Tyr His Thr Met Pro Pro Gln 65 70 75 80

Pro Gly Met Pro Ala Ala Pro Tyr Pro Met Gln Tyr Pro Pro Pro Tyr

85 90 95

Pro Ala Gln Pro Met Gly Pro Pro Ala Tyr His Glu Thr Leu Ala Gly
100 105 110

Glu Cys Pro Cys Gln Leu 115

<210> 32

<211> 1908

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (91).. (444)

<400> 32

gggggaggaa attgaaactg agtggcccac gatgggaaga ggggaaagcc caggggtaca 60 83/735

gga	ggcc	tct	gggt	gaag	gc a	gagg	ctaa								g gcc u Ala	114
									1	,			5			
									•				•			
gtt	ggc	ctg	acc	atc	ttt	gtg	ctg	tct	gtc	gtc	act	atc	atc	atc	tgc	162
Val	Gly	Leu	Thr	Ile	Phe	Val	Leu	Ser	Val	Val	Thr	Ile	Ile	Ile	Cys	
	10					15					20					
ttc	acc	tgc	tcc	tgc	tgc	tgc	ctt	tac	aag	acg	tgc	cgc	cga	cca	cgt	210
		_	_	_	_	_	_	_	_		_			Pro		
25					30					35					40	
ccg	gtt	gtc	acc	acc	acc	aca	tcc	acc	act	gtg	gtg	cat	gcc	cct	tat	258
Pro	Val	Val	Thr	Thr	Thr	Thr	Ser	Thr	Thr	Val	Val	His	Ala	Pro	Tyr	
				45					50					55		
cct	cag	cct	cca	agt	gtg	ccg	ccc	agc	tac	cct	gga	cca	agc	tac	cag	306
Pro	Gln	Pro	Pro	Ser	Val	Pro	Pro	Ser	Tyr	Pro	Gly	Pro	Ser	Tyr	Gln	
			60					65					70			
ggc	tac	cac	acc	atg	ccg	cct	cag	cca	ggg	atg	cca	gca	gca	ccc	tac	354
Gly	Tyr	His	Thr	Met	Pro	Pro	Gln	Pro	Gly	Met	Pro	Ala	Ala	Pro	Tyr	
		75					80					85				
cca	atg	cag	tac	cca	cca	cct	tac	cca	gcc	cag	ccc	atg	ggc	cca	ccg	402
Pro	Met	Gln	Tyr	Pro	Pro	Pro	Tyr	Pro	Ala	Gln	Pro	Met	Gly	Pro	Pro	
	90					95					100					

gcc tac cac gag acc ctg gct ggt gag tgc ccc tgc caa ctc

444

Ala Tyr His Glu Thr Leu Ala Gly Glu Cys Pro Cys Gln Leu

105

110

115

tagccctgcc cgacttcccg agtctctgcc agcatccctc gggcacccat cccaaactac 504 atcactcaac aggectetge ecetttetge ttgcetgeca etcacaegge ageceaceat 564 getcacagee aaccagggte etetetgett teaggaggag cageegegee etaceeegee 624 agccagcete ettacaacce ggeetacatg gatgeecega aggeggeect etgageatte 684 cctggcctct ctggctgcca cttggttatg ttgtgtgtgt gcgtgagtgg tgtgcaggcg 744 cggttcctta cgccccatgt gtgctgtgtg tgtccaggca cggttcctta cgccccatgt 804 gtgctgtgtg tgtcctgcct gtatatgtgg cttcctctga tgctgacaag gtggggaaca 864 atcettgeea gagtgggetg ggaccagaet ttgttetett ceteacetga aattatgett 924 cctaaaatct caagccaaac tcaaagaatg gggtggtggg gggcaccctg tgaggtggcc 984 cctgagaggt gggggcctct ccagggcaca tctggagttc ttctccagct taccctaggg 1044 tgaccaagta gggcctgtca caccagggtg gcgcagcttt ctgtgtgatg cagatgtgtc 1104 ctggtttcgg cagcgtagcc agctgctgct tgaggccatg gctcgtcccc ggagttgggg 1164 gtacccgttg cagagccagg gacatgatgc aggcgaagct tgggatctgg ccaagttgga 1224 85/735

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<210> 33

<211> 168

<212> PRT

<213> Homo sapiens

<400> 33

 $\hbox{Met Asn Ser Lys Gly Gln Tyr Pro Thr Gln Pro Thr Tyr Pro Val Gln } \\$

1 5 10 15

Pro Pro Gly Asn Pro Val Tyr Pro Gln Thr Leu His Leu Pro Gln Ala

20 25 30

Pro Pro Tyr Thr Asp Ala Pro Pro Ala Tyr Ser Glu Leu Tyr Arg Pro

35 40 45

Ser Phe Val His Pro Gly Ala Ala Thr Val Pro Thr Met Ser Ala Ala

50 55 60

Phe Pro Gly Ala Ser Leu Tyr Leu Pro Met Ala Gln Ser Val Ala Val

65 70 75 80

Gly Pro Leu Gly Ser Thr Ile Pro Met Ala Tyr Tyr Pro Val Gly Pro

85 90 95

Ile Tyr Pro Pro Gly Ser Thr Val Leu Val Glu Gly Gly Tyr Asp Ala

100 105 110

Gly Ala Arg Phe Gly Ala Gly Ala Thr Ala Gly Asn Ile Pro Pro Pro

115 120 125

Pro Pro Gly Cys Pro Pro Asn Ala Ala Gln Leu Ala Val Met Gln Gly

130 135 140

87/735

Ala Asn Val Leu Val Thr Gln Arg Lys Gly Asn Phe Phe Met Gly Gly
145 150 155 160

Ser Asp Gly Gly Tyr Thr Ile Trp 165

<210> 34

<211> 1897

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (70).. (573)

<400> 34

ctccgaacag gaagaggacg aaaaaaataa ccgtccgcga cgccgagaca aaccggaccc 60

gcaaccacc atg aac agc aaa ggt caa tat cca aca cag cca acc tac cct 111

Met Asn Ser Lys Gly Gln Tyr Pro Thr Gln Pro Thr Tyr Pro

1 5 10

gtg cag cct cct ggg aat cca gta tac cct cag acc ttg cat ctt cct 159
Val Gln Pro Pro Gly Asn Pro Val Tyr Pro Gln Thr Leu His Leu Pro
15 20 25 30

cag gct cca ccc tat acc gat gct cca cct gcc tac tca gag ctc tat 207 88/735

Gln	Ala	Pro	Pro	Tyr	Thr	Asp	Ala	Pro	Pro	Ala	Tyr	Ser	G1u	Leu	Tyr	
				35					40					45		
cgt	ccg	agc	ttt	gtg	cac	cca	ggg	gct	gcc	aca	gtc	ccc	acc	atg	tca	255
Arg	Pro	Ser	Phe	Val	His	Pro	Gly	Ala	Ala	Thr	Val	Pro	Thr	Met	Ser	
			50					55					60			
gcc	gca	ttt	cct	gga	gcc	tct	ctg	tat	ctt	ccc	atg	gcc	cag	tct	gtg	303
Ala	Ala	Phe	Pro	Gly	Ala	Ser	Leu	Tyr	Leu	Pro	Met	Ala	Gln	Ser	Val	
		65					70					75				
		•													•	
gct	gtt	ggg	cct	tta	ggt	tcc	aca.	atc	ссс	atg	gct	tat	tat	cca	gtc	351
Ala	Val	Gly	Pro	Leu	Gly	Ser	Thr	Ile	Pro	Met	Ala	Tyr	Tyr	Pro	Val	
	80					85					90					
ggt	ccc	atc	tat	cca	cct	ggc	tcc	aca	gtg	ctg	gtg	gaa	gga	ggg	tat	399
Gly	Pro	Ile	Tyr	Pro	Pro	G1y	Ser	Thr	Val	Leu	Val	Glu	Gly	Gly	Tyr	
95					100					105					110	
gat	gca	ggt	gcc	aga	ttt	gga	gct	ggg	gct	act	gct	ggc	aac	att	cct	447
Asp	Ala	Gly	Ala	Arg	Phe	Gly	Ala	Gly	Ala	Thr	Ala	G1y	Asn	Ile	Pro	
				115					120					125		
cct	cca	cct	cct	gga	tgc	cct	ccc	aat	gct	gct	cag	ctt	gca	gtc	atg	495
Pro	Pro	Pro	Pro	Gly	Cys	Pro	Pro	Asn	Ala	Ala	Gln	Leu	Ala	Val	Met	
			130					135					140			
cag	gga	gcc	aac	gtc	ctc	gta	act	cag	cgg	aag	ggg	aac	ttc	ttc	atg	543
Gln	Gly	Ala	Asn	Val	Leu	Val	Thr		_	Lys	Gly	Asn	Phe	Phe	Met	
								89/	133							

145 150 155

ggt ggt tca gat ggt ggc tac acc atc tgg tgaggaacca aggccacctc 593
Gly Gly Ser Asp Gly Gly Tyr Thr Ile Trp
160 165

tgtgccggga aagacatcac ataccttcag cacttctcac aatgtaactg ctttagtcat 653 attaacctga agttgcagtt tagacacatg ttgttggggt gtctttctgg tgcccaaact 713 ttcaggcact tttcaaattt aataaggaac catgtaatgg tagcagtacc tccctaaagc 773 attttgaggt aggggaggta tccattcata aaatgaatgt gggtgaagcc gccctaagga 833 ttttccttta atttctctgg agtaatactg taccatactg gtctttgctt ttagtaataa 893 aacatcaaat taggtttgga gggaactttg atcttcctaa gaattaaagt tgccaaatta 953 ttctgattgg tctttaatct cctttaagtc tttgatatat attacttgtt ataaatggaa 1013 cgcattagtt gtctgccttt tcctttccat cccttgcccc acccatccca tctccaaccc 1073 tagtetteea ttteeteeg eeagteteea ttgaateaat ggtgeaggae agaaageeag 1133 teagactaat tteettettt eetegeactt eteceeacte gteatetttt aactagtgtt 1193 tcacaaggat cctctgaaac cctctctgtg ccccaagtac agatgccatt acttctgctt 1253 tcgtatctcc tcaggcaaaa gtggagggtg ccttatgggc cctcctcata ggttgtctct 1313 90/735

gcatacacga acctaaccca aatttgettt ggtgccagaa aaactgaget atgtttgaac 1373

aaagatgteg tgcaaactgt actgtgaaca acagttggtt taaaatatga ggggcaagga 1433

ggaggatgca tttcaaaage ttgattgatg tgttcagage taaattaaga ggagttttea 1493

gatcaaaaac tggttaccat tttttgtcag agtgtctgat geggccacte atteggetee 1553

ccagaattee tagactgggt taatagggte atattgtgaa tgtctcacta caaaatgact 1613

tgagtccagt gaaateteat tagggtttaa gaatattea gggatcetta atgtttgat 1673

ttttgttte tgaaattgga ttttattta ttttatetta taattteagt teatetaaat 1733

tgtgtgttet gtacatgtga tgtttgactg taccattgae tgttatggaa gttcagegtt 1793

gtatgteet etetacactg tggtgcactt aacttgtgga attttatae taaaaatgta 1853

gaataaagae tattttgaag atttgaataa agtgatgaag ttge 1897

<210> 35

<211> 455

<212> PRT

<213> Homo sapiens

<400> 35

Met Ser Phe Leu Ile Asp Ser Ser Ile Met Ile Thr Ser Gln Ile Leu 91/735

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1 C 1/3

1 5 10 15

Phe Phe Gly Phe Gly Trp Leu Phe Phe Met Arg Gln Leu Phe Lys Asp
20 25 30

Tyr Glu Ile Arg Gln Tyr Val Val Gln Val Ile Phe Ser Val Thr Phe
35 40 45

Ala Phe Ser Cys Thr Met Phe Glu Leu Ile Ile Phe Glu Ile Leu Gly
50 55 60

Val Leu Asn Ser Ser Ser Arg Tyr Phe His Trp Lys Met Asn Leu Cys
65 70 75 80

Val Ile Leu Leu Ile Leu Val Phe Met Val Pro Phe Tyr Ile Gly Tyr

85 90 95

Phe Ile Val Ser Asn Ile Arg Leu Leu His Lys Gln Arg Leu Leu Phe 100 105 110

Ser Cys Leu Leu Trp Leu Thr Phe Met Tyr Phe Phe Trp Lys Leu Gly
115 120 125

Asp Pro Phe Pro Ile Leu Ser Pro Lys His Gly Ile Leu Ser Ile Glu 130 135 140

Gln Leu Ile Ser Arg Val Gly Val Ile Gly Val Thr Leu Met Ala Leu 145 150 155 160

Leu Ser Gly Phe Gly Ala Val Asn Cys Pro Tyr Thr Tyr Met Ser Tyr

165 170 175

Phe Leu Arg Asn Val Thr Asp Thr Asp Ile Leu Ala Leu Glu Arg Arg 180 185 190

Leu Leu Gln Thr Met Asp Met IIe IIe Ser Lys Lys Lys Arg Met Ala 195 200 205

Met Ala Arg Arg Thr Met Phe Gln Lys Gly Glu Val His Asn Lys Pro 210 215 220

Ser Gly Phe Trp Gly Met Ile Lys Ser Val Thr Thr Ser Ala Ser Gly
225 230 235 240

Ser Glu Asn Leu Thr Leu Ile Gln Gln Glu Val Asp Ala Leu Glu Glu
245 250 255

Leu Ser Arg Gln Leu Phe Leu Glu Thr Ala Asp Leu Tyr Ala Thr Lys
260 265 270

Glu Arg Ile Glu Tyr Ser Lys Thr Phe Lys Gly Lys Tyr Phe Asn Phe 275 280 285

Leu Gly Tyr Phe Phe Ser Ile Tyr Cys Val Trp Lys Ile Phe Met Ala 290 295 300

Thr Ile Asn Ile Val Phe Asp Arg Val Gly Lys Thr Asp Pro Val Thr

305 310 315 320

93/735

Arg Gly Ile Glu Ile Thr Val Asn Tyr Leu Gly Ile Gln Phe Asp Val
325 330 335

Lys Phe Trp Ser Gln His Ile Ser Phe Ile Leu Val Gly Ile Ile Ile 340 345 350

Val Thr Ser Ile Arg Gly Leu Leu Ile Thr Leu Thr Lys Phe Phe Tyr 355 360 365

Ala Ile Ser Ser Ser Lys Ser Ser Asn Val Ile Val Leu Leu Leu Ala 370 375 380

Gln Ile Met Gly Met Tyr Phe Val Ser Ser Val Leu Leu Ile Arg Met 385 390 395 400

Ser Met Pro Leu Glu Tyr Arg Thr Ile Ile Thr Glu Val Leu Gly Glu
405 410 415

Leu Gln Phe Asn Phe Tyr His Arg Trp Phe Asp Val Ile Phe Leu Val
420 425 430

Ser Ala Leu Ser Ser Ile Leu Phe Leu Tyr Leu Ala His Lys Gln Ala 435 440 445

Pro Glu Lys Gln Met Ala Pro 450 455

<210> 36

<211> 1903

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (116).. (1480)

20

<400> 36

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tgctgtggcc tcggggagtg ggaagtggag gcaggagcct tccttacact tcgcc atg 118

. 1

agt ttc ctc atc gac tcc agc atc atg att acc tcc cag ata cta ttt 166

Ser Phe Leu Ile Asp Ser Ser Ile Met Ile Thr Ser Gln Ile Leu Phe

5 10 15

ttt gga ttt ggg tgg ctt ttc ttc atg cgc caa ttg ttt aaa gac tat 214
Phe Gly Phe Gly Trp Leu Phe Phe Met Arg Gln Leu Phe Lys Asp Tyr

30

25

gag ata cgt cag tat gtt gta cag gtg atc ttc tcc gtg acg ttt gca 262
Glu Ile Arg Gln Tyr Val Val Gln Val Ile Phe Ser Val Thr Phe Ala
35 40 45

ttt tct tgc acc atg ttt gag ctc atc ttt gaa atc tta gga gta 310 95/735

W	O 02/	05373	37												PCT/	JP01/11389
Phe	Ser	Cys	Thr	Met	Phe	Glu	Leu	Ile	Ile	Phe	Glu	Ile	Leu	Gly	Val	
50					55					60					65	
ttg	aat	agc	agc	tcc	cgt	tat	ttt	cac	tgg	aaa	atg	aac	ctg	tgt	gta	358
Leu	Asn	Ser	Ser	Ser	Arg	Tyr	Phe	His	Trp	Lys	Met	Asn	Leu	Cys	Val	
				70					75					80		
att	ctg	ctg	atc	ctg	gtt	ttc	atg	gtg	cct	ttt	tac	att	ggc	tat	ttt	406
	_	_		Leu	_		_									
			85					90					95			
															•	
att	gtg	agc	aat	atc	cga	cta	ctg	cat	aaa	caa	cga	ctg	ctt	ttt	tcc	454
Ile	Val	Ser	Asn	Ile	Arg	Leu	Leu	His	Lys	Gln	Arg	Leu	Leu	Phe	Ser	
		100					105					110				
tgt	ctc	tta	tgg	ctg	acc	ttt	atg	tat	ttc	ttc	tgg	aaa	cta	gga	gat	502
Cys	Leu	Leu	Trp	Leu	Thr	Phe	Met	Tyr	Phe	Phe	Trp	Lys	Leu	Gly	Asp	
	115					120					125					
																550
				ctc	_									_	_	550
130	rne	Pro	TTE	Leu	3er 135	Pro	Lys	nis	GIY	140	Leu	ser	TTE	GIU	145	
100					100					1-10					140	
ctc	atc	agc	cgg	gtt	ggt	gtg	att	gga	gtg	act	ctc	atg	gct	ctt	ctt	598

tct gga ttt ggt gct gtc aac tgc cca tac act tac atg tct tac ttc 646 Ser Gly Phe Gly Ala Val Asn Cys Pro Tyr Thr Tyr Met Ser Tyr Phe 96/735

155

160

Leu Ile Ser Arg Val Gly Val Ile Gly Val Thr Leu Met Ala Leu Leu

150

			165					170					175			
													cgg Arg			694
		180					185					190				
ctg	caa	acc	atg	gat	atg	atc	ata	agc	aaa	aag	aaa	agg	atg	gca	atg	742
Leu	Gln	Thr	Met	Asp	Met	Ile	Ile	Ser	Lys	Lys	Lys	Arg	Met	Ala	Met	
	195					200					205					

gca cgg aga aca atg ttc cag aag ggg gaa gtg cat aac aaa cca tca 790
Ala Arg Arg Thr Met Phe Gln Lys Gly Glu Val His Asn Lys Pro Ser
210 215 220 225

ggt ttc tgg gga atg ata aaa agt gtt acc act tca gca tca gga agt 838 Gly Phe Trp Gly Met Ile Lys Ser Val Thr Thr Ser Ala Ser Gly Ser 230 235 240

gaa aat ctt act ctt att caa cag gaa gtg gat gct ttg gaa gaa tta 886 Glu Asn Leu Thr Leu Ile Gln Gln Glu Val Asp Ala Leu Glu Glu Leu 245 250 255

agc agg cag ctt ttt ctg gaa aca gct gat cta tat gct acc aag gag 934 Ser Arg Gln Leu Phe Leu Glu Thr Ala Asp Leu Tyr Ala Thr Lys Glu 260 265 270

aga ata gaa tac tcc aaa acc ttc aag ggg aaa tat ttt aat ttt ctt 982
Arg Ile Glu Tyr Ser Lys Thr Phe Lys Gly Lys Tyr Phe Asn Phe Leu
275 280 285

ggt	tac	ttt	ttc	tct	att	tac	tgt	gtt	tgg	aaa	att	ttc	atg	gct	acc	1030
G1y	Tyr	Phe	Phe	Ser	Ile	Tyr	Cys	Val	Trp	Lys	Ile	Phe	Met	Ala	Thr	
290					295					300					305	
atc	aat	att	gtt	ttt	gat	cga	gtt	ggg	aaa	acg	gat	cct	gtc	aca	aga	1078
Ile	Asn	Ile	Val	Phe	Asp	Arg	Val	Gly	Lys	Thr	Asp	Pro	Val	Thr	Arg	
				310					315					320		
ggc	att	gag	atc	act	gtg	aat	tat	ctg	gga	atc	caa	ttt	gat	gtg	aag	1126
Gly	Ile	G1u	Ile	Thr	Val	Asn	Tyr	Leu	Gly	Ile	Gln	Phe	Asp	Val	Lys	
			325					330					335			
ttt	tgg	tcc	caa	cac	att	tcc	ttc	att	ctt	gtt	gga	ata	atc	atc	gtc	1174
Phe	Trp	Ser	G1n	His	Ile	Ser	Phe	Ile	Leu	Val	Gly	Ile	Ile	Ile	Va1	
		340					345					350				
•																
aca	tcc	atc	aga	gga	ttg	ctg	atc	act	ctt	acc	aag	ttc	ttt	tat	gcc	1222
Thr	Ser	Ile	Arg	Gly	Leu	Leu	Ile	Thr	Leu	Thr	Lys	Phe	Phe	Tyr	Ala	
	355					360					365					
atc	tct	agc	agt	aag	tcc	tcc	aat	gtc	att	gtc	ctg	cta	tta	gca	cag	1270
Ile	Ser	Ser	Ser	Lys	Ser	Ser	Asn	Val	Ile	Val	Leu	Leu	Leu	Ala	Gln	
370					375					380					385	
ata	atg	ggc	atg	tac	ttt	gtc	tcc	tct	gtg	ctg	ctg	atc	cga	atg	agt	1318
Ile	Met	G1y	Met	Tyr	Phe	Val	Ser	Ser	Val	Leu	Leu	Ile	Arg	Met	Ser	
				390					395					400		

atg cct tta gaa tac cgc acc ata atc act gaa gtc ctt gga gaa ctg 1366
Met Pro Leu Glu Tyr Arg Thr Ile Ile Thr Glu Val Leu Gly Glu Leu
405 410 415

cag ttc aac ttc tat cac cgt tgg ttt gat gtg atc ttc ctg gtc agc 1414
Gln Phe Asn Phe Tyr His Arg Trp Phe Asp Val Ile Phe Leu Val Ser
420 425 430

gct ctc tct agc ata ctc ttc ctc tat ttg gct cac aaa cag gca cca 1462
Ala Leu Ser Ser Ile Leu Phe Leu Tyr Leu Ala His Lys Gln Ala Pro
435 440 445

gag aag caa atg gca cct tgaacttaag cctactacag actgttagag 1510
Glu Lys Gln Met Ala Pro
450 455

gecagtggtt teaaaattta gatataagag gggggaaaaa tggaaceag geetgacatt 1570
ttataaacaa acaaaatget atggtageat tttteacett catageatae teetteeceg 1630
teaggtgata etatgaceat gagtageate ageeagaaca tgagagggag aactaactea 1690
agacaataet cageagagag cateeegtg ggatatgagg etggtgtaga ggeggagagg 1750
ageeaagaaa etaaaggtga aaaatacaet ggaactetgg ggeaagaeat gtetatggta 1810
getgageeaa acaegtagga ttteegtttt aaggtteaca tggaaaaggt tatagetttg 1870

ccttgagatt gactcattaa aatcagagac tgt 1903 99/735

<210> 37

<211> 322

<212> PRT

<213> Homo sapiens

20

<400> 37

Met Ser Ser Leu Gly Gly Gly Ser Gln Asp Ala Gly Gly Ser Ser Ser

1 5 10 15

Ser Ser Thr Asn Gly Ser Gly Gly Ser Gly Ser Gly Pro Lys Ala

25

30

Gly Ala Ala Asp Lys Ser Ala Val Val Ala Ala Ala Ala Pro Ala Ser 35 40 45

Val Ala Asp Asp Thr Pro Pro Pro Glu Arg Arg Asn Lys Ser Gly Ile
50 55 60

Ile Ser Glu Pro Leu Asn Lys Ser Leu Arg Arg Ser Arg Pro Leu Ser
65 70 75 80

His Tyr Ser Ser Phe Gly Ser Ser Gly Gly Ser Gly Gly Ser Met
85 90 95

Met Gly Glu Ser Ala Asp Lys Ala Thr Ala Ala Ala Ala Ala Ala 100 105 110

100/735

Ser	Leu		Ala	Asn	Gly	His	Asp 120	Leu	Ala	Ala	Ala	Met 125	Ala	Val	Asp
		115					120					120			
Lys	Ser	Asn	Pro	Thr	Ser	Lys	His	Lys	Ser	Gly	Ala	Val	Ala	Ser	Leu
	130					135					140				
Leu	Ser	Lys	Ala	Glu	Arg	Ala	Thr	Glu	Leu	Ala	Ala	Glu	Gly	Gln	Leu
145					150					155					160
Thr	Leu	G1n	G1n	Phe	Ala	Gln	Ser	Thr	Glu	Met	Leu	Lys	Arg	Val	Val
				165					170					175	
C1	C1	W	I	Desc	Lau	Mat.	Com	Clu	Αla	C1	۸۱۵	C1**	Lou	Dro	Aan
GIN	GIU	nıs	180	Pro	Leu	Mer		·185	ніа	Gly	ита	Gly	190	710	nsp
Met	Glu	Ala 195	Val	Ala	Gly	Ala	Glu 200	Ala	Leu	Asn	Gly	Gln 205	Ser	Asp	Phe
		100													
Pro		Leu	Gly	Ala	Phe		Ile	Asn	Pro	Gly		Phe	Ile	Met	Thr
	210					215					220				
Pro	Ala	Gly	Val	Phe	Leu	Ala	Glu	Ser	Ala	Leu	His	Met	Ala	Gly	Leu
225					230					235					240
Ala	Glu	Tyr	Pro	Met	G1n	Gly	Glu	Leu	Ala	Ser	Ala	Ile	Ser	Ser	Gly
				245					250					255	·
Ive	Lve	Lvs	Arø	Lvs	Arg	Cvs	G1 v	Met	Cvs	A1a	Pro	Cvs	Arg	Arø	Arø
<i>د و ب</i>	ں رہ	ت ر ـــ		_,_	0	-,5	7		-,5			. , -	0	0	0

265

101/735

260

270

Ile Asn Cys Glu Gln Cys Ser Ser Cys Arg Asn Arg Lys Thr Gly His
275 280 285

Gln Ile Cys Lys Phe Arg Lys Cys Glu Glu Leu Lys Lys Lys Pro Ser 290 295 300

Ala Ala Leu Glu Lys Val Met Leu Pro Thr Gly Ala Ala Phe Arg Trp 305 310 315 320

Phe Gln

<210> 38

<211> 1448

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (292).. (1257)

<400> 38

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ccctgcccg ccctcccc teggcctcge ggcgacggcg geggtggcgg cttggacgac 120

tcggagagcc gagtgaagac atttccacct ggacacctga ccatgtgcct gccctgagca 180 102/735

gcg	aggc	cca	ccag	gcat	ct c	tgtt	gtgg	g ca	gcag	ggcc	agg	tcct	ggt	ctgt	ggaccc	240
tcg	gcag	ttg	gcag	gctc	cc t	ctgc	agtg	g gg	tctg	ggcc	tcg	gccc	cac	Me	g tcg t Ser	297
agc	ctc	ggc	ggt	ggc	tcc	cag	gat	gcc	ggc	ggc	agt	agc	agc	agc	agc	345
Ser	Leu	G1y	Gly	Gly	Ser	Gln	Asp	Ala	Gly	Gly	Ser	Ser	Ser	Ser	Ser	
		5					10					15				
acc	aat	ggc	agc	ggt	ggc	agt	ggc	agc	agt	ggc	cca	aag	gca	gga	gca	393
Thr	Asn	Gly	Ser	Gly	Gly	Ser	Gly	Ser	Ser	Gly	Pro	Lys	Ala	Gly	Ala	
	20					25					30					
gca	gac	aag	agt	gca	gtg	gtg	gct	gcc	gcc	gca	cca	gcc	tca	gtg	gca	441
Ala	Asp	Lys	Ser	Ala	Val	Val	Ala	Ala	Ala	Ala	Pro	Ala	Ser	Val	Ala	
35					40					45					50	
gat.	gac	aca	cca	ccc	ccc	gag	cet	CEE	aac	aag	agc	ggt.	atc	atc	agt.	489
			Pro													
				55		-	0	0	60	-•-		,		65		
gag	ccc	ctc	aac	aag	agc	ctg	cgc	cgc	tcc	cgc	ccg	ctc	tcc	cac	tac	537
Glu	Pro	Leu	Asn	Lys	Ser	Leu	Arg	Arg	Ser	Arg	Pro	Leu	Ser	His	Tyr	
			70					75					80			
+++	tot	+++	ggc	900	ar+	aa+	uu+	a (r+	aao	aa+	aav	200	a+~	at~	aac	585
														_		585
ser	Set.	rne	Gly	Set	oer	GIÀ	GTÀ	103/		GIY	GIÀ	ser	мет	met	ΩŢÃ	

		85					90					95				
gga	gag	tct	gct	gac	aag	gcc	act	gcg	gct	gca	gcc	gct	gcc	tcc	ctg	633
Gly	Glu	Ser	Ala	Asp	Lys	Ala	Thr	Ala	Ala	Ala	Ala	Ala	Ala	Ser	Leu	
	100					105					110					
ttg	gcc	aat	ggg	cat	gac	ctg	gcg	gcg	gcc	atg	gcg	gtg	gac	aaa	agc	681
Leu	Ala	Asn	G1y	His	Asp	Leu	Ala	Ala	Ala	Met	Ala	Val	Asp	Lys	Ser	
115					120					125					130	
aac	cct	acc	tca	aag	cac	aaa	agt	ggt	gct	gtg	gcc	agc	ctg	ctg	agc	729
Asn	Pro	Thr	Ser	Lys	His	Lys	Ser	Gly	Ala	Val	Ala	Ser	Leu	Leu	Ser	
				135					140					145		
aag	gca	gag	cgg	gcc	acg	gag	ctg	gca	gcc	gag	gga	cag	ctg	acg	ctg	777
Lys	Ala	Glu	Arg	Ala	Thr	Glu	Leu	Ala	Ala	Glu	Gly	Gln	Leu	Thr	Leu	
			150					155					160			
cag	cag	ttt	gcg	cag	tcc	aca	gag	atg	ctg	aag	cgc	gtg	gtg	cag	gag	825
														Gln		
		165					170			_,_	0	175				
		100														
cat	ctc	cca	cta	ato	age	gag	aca	σσt	øct	ggc	ctø	cct	gac	atg	gag	873
														Met		0.0
1113	180	110	Leu	Mec	001	185	пта	Oly	nia	Oly	190	110	пор	MC C	Olu	
	100					100					130					
ac+	at-		~~+	~cc	aee	ac.	a+-	o.c.+	~~	000	too	asc	++^	000	tac	921
														CCC		36I
	vaı	ита	GTÀ	ита		ита	Leu	Asn	GΙΆ		ser	кѕр	rne	Pro		
195					200					205					210	

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WO 02/053737

PCT/JP01/11389

ctg	ggc	gct	ttc	ссс	atc	aac	cca	ggc	ctc	ttc	att	atg	acc	ccg	gca	969
Leu	Gly	Ala	Phe	Pro	Ile	Asn	Pro	Gly	Leu	Phe	Ile	Met	Thr	Pro	Ala	
				215					220					225		
ggt	gtg	ttc	ctg	gcc	gag	agc	gcg	ctg	cac	atg	gcg	ggc	ctg	gct	gag	1017
Gly	Val	Phe	Leu	Ala	Glu	Ser	Ala	Leu	His	Met	Ala	Gly	Leu	Ala	Glu	
			230					235					240			
tac	ccc	atg	cag	gga	gag	ctg	gcc	tct	gcc	atc	agc	tcc	ggc	aag	aag	1065
Tyr	Pro	Met	Gln	Gly	Glu	Leu	Ala	Ser	Ala	Ile	Ser	Ser	Gly	Lys	Lys	
		245					250					255				
aag	cgg	aaa	cgc	tgc	ggc	atg	tgc	gcg	ccc	tgc	cgg	cgg	cgc	atc	aac	1113
Lys	Arg	Lys	Arg	Cys	Gly	Met	Cys	Ala	Pro	Cys	Arg	Arg	Arg	Ile	Asn	
	260					265					270					
tgc	gag	cag	tgc	agc	agt	tgt	agg	aat	cga	aag	act	ggc	cat	cag	att	1161
Cys	G1u	G1n	Cys	Ser	Ser	Cys	Arg	Asn	Arg	Lys	Thr	Gly	His	G1n	Ile	
275					280					285					290	
tgc	aaa	ttc	aga	aaa	tgt	gag	gaa	ctc	aaa	aag	aag	cct	tcc	gct	gct	1209
Cys	Lys	Phe	Arg	Lys	Cys	Glu	Glu	Leu	Lys	Lys	Lys	Pro	Ser	Ala	Ala	•
				295					300					305		
ctg	gag	aag	gtg	atg	ctt	ccg	acg	gga	gcc	gcc	ttc	cgg	tgg	ttt	cag	1257
Leu	G1u	Lys	Val	Met	Leu	Pro	Thr	Gly	Ala	Ala	Phe	Arg	Trp	Phe	G1n	
			310					315					320			

tgacggcggc ggaacccaaa gctgccctct ccgtgcaatg tcactgctcg tgtggtctcc 1317

agcaagggat tcgggcgaag acaaacggat gcacccgtct ttagaaccaa aaatattctc 1377

tcacagattt cattcctgtt tttatatata tattttttgt tgtcgtttta acatctccac 1437

gtccctagca t 1448

<210> 39

<211> 313

<212> PRT

<213> Homo sapiens

<400> 39

Met Ala Gly Gln Pro Gly His Met Pro His Gly Gly Ser Ser Asn Asn

1 5 10 15

Leu Cys His Thr Leu Gly Pro Val His Pro Pro Asp Pro Gln Arg His
20 25 30

Pro Asn Thr Leu Ser Phe Arg Cys Ser Leu Ala Asp Phe Gln Ile Glu 35 40 45

Lys Lys Ile Gly Arg Gly Gln Phe Ser Glu Val Tyr Lys Ala Thr Cys
50 55 60

Leu Leu Asp Arg Lys Thr Val Ala Leu Lys Lys Val Gln Ile Phe Glu 65 70 75 80 106/735

Met Met Asp Ala Lys Ala Arg Gln Asp Cys Val Lys Glu Ile Gly Leu 85 90 95

Leu Lys Gln Leu Asn His Pro Asn Ile Ile Lys Tyr Leu Asp Ser Phe
100 105 110

Ile Glu Asp Asn Glu Leu Asn Ile Val Leu Glu Leu Ala Asp Ala Gly
115 120 125

Asp Leu Ser Gln Met Ile Lys Tyr Phe Lys Lys Gln Lys Arg Leu Ile 130 135 140

Pro Glu Arg Thr Val Trp Lys Tyr Phe Val Gln Leu Cys Ser Ala Val 145 150 155 160

Glu His Met His Ser Arg Arg Val Met His Arg Asp Ile Lys Pro Ala 165 170 175

Asn Val Phe Ile Thr Ala Thr Gly Val Val Lys Leu Gly Asp Leu Gly
180 185 190

Leu Gly Arg Phe Phe Ser Ser Glu Thr Thr Ala Ala His Ser Leu Val 195 200 205

Gly Thr Pro Tyr Tyr Met Ser Pro Glu Arg Ile His Glu Asn Gly Tyr 210 215 220

Asn Phe Lys Ser Asp Ile Trp Ser Leu Gly Cys Leu Leu Tyr Glu Met 107/735

225 230 235 240

Ala Ala Leu Gln Ser Pro Phe Tyr Gly Asp Lys Met Asn Leu Phe Ser

245 250 255

Leu Cys Gln Lys Ile Glu Gln Cys Asp Tyr Pro Pro Leu Pro Gly Glu 260 265 270

His Tyr Ser Glu Lys Leu Arg Glu Leu Val Ser Met Cys Ile Cys Pro 275 280 285

Asp Pro His Gln Arg Pro Asp Ile Gly Tyr Val His Gln Val Ala Lys 290 295 300

Gln Met His Ile Trp Met Ser Ser Thr 305 310

<210> 40

<211> 1597

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (153).. (1091)

<400> 40

ggcggaaccg agctgacggg cgtgcggccg ctgcgccgca aactcgtgtg ggacgcaccg 60 108/735

ctc	cagco	cgc	ccgcį	gggc	ca go	cgca	ccggt	cce	cca	gcgg	cage	ccga	gcc	cgcc	cgcgcg	120
ccgt	ttcg	tgc (cctcį	gtgag	gg ci	tggca	atgca	ı gg						ggc Gly		173
									1				5			
atg	ccc	cat	gga	ggg	agt	tcc	aac	aac	ctc	tgc	cac	acc	ctg	ggg	cct	221
Met	Pro	His	Gly	Gly	Ser	Ser	Asn	Asn	Leu	Cys	His	Thr	Leu	Gly	Pro	
		10					15					20				
gtg	cat	cct	cct	gac	cca	cag	agg	cat	ccc	aac	acg	ctg	tct	ttt	cgc	269
Val	His	Pro	Pro	Asp	Pro	Gln	Arg	His	Pro	Asn	Thr	Leu	Ser	Phe	Arg	
	25					30					35					
tgc	tcg	ctg	gcg	gac	ttc	cag	atc	gaa	aag	aag	ata	ggc	cga	gga	cag	317
Cys	Ser	Leu	Ala	Asp	Phe	Gln	Ile	G1u	Lys	Lys	Ile	Gly	Arg	Gly	Gln	
40					45					50					55	
ttc	agc	gag	gtg	tac	aag	gcc	acc	tgc	ctg	ctg	gac	agg	aag	aca	gtg .	365
Phe	Ser	Glu	Val	Tyr	Lys	Ala	Thr	Cys	Leu	Leu	Asp	Arg	Lys	Thr	Val	
				60					65					70		
gct	ctg	aag	aag	gtg	cag	atc	ttt	gag	atg	atg	gac	gcc	aag	gcg	agg	413
Ala	Leu	Lys	Lys	Val	Gln	Ile	Phe	Glu	Met	Met	Asp	Ala	Lys	Ala	Arg	
			75					80					85		•	
cag	gac	tgt	gtc	aag	gag	atc	ggc	ctc	ttg	aag	caa	ctg	aac	cac	cca	461
Gln	Asp	Cys	.Val	Lys	Glu	Ile	Gly	Leu 109		Lys	Gln	Leu	Asn	His	Pro	

90 95 100

aat atc atc aag tat ttg gac tcg ttt atc gaa gac aac gag ctg aac 509

Asn Ile Ile Lys Tyr Leu Asp Ser Phe Ile Glu Asp Asn Glu Leu Asn

115

att gtg ctg gag ttg gct gac gca ggg gac ctc tcg cag atg atc aag 557

Ile Val Leu Glu Leu Ala Asp Ala Gly Asp Leu Ser Gln Met Ile Lys

120 125 130 135

110

105

tac ttt aag aag cag aag cgg ctc atc ccg gag agg aca gta tgg aag 605

Tyr Phe Lys Lys Gln Lys Arg Leu Ile Pro Glu Arg Thr Val Trp Lys

140 145 150

tac ttt gtg cag ctg tgc agc gcc gtg gag cac atg cat tca cgc cgg 653

Tyr Phe Val Gln Leu Cys Ser Ala Val Glu His Met His Ser Arg Arg

155 160 165

gtg atg cac cga gac atc aag cct gcc aac gtg ttc atc aca gcc acg 701
Val Met His Arg Asp Ile Lys Pro Ala Asn Val Phe Ile Thr Ala Thr
170 175 180

ggc gtc gtg aag ctc ggt gac ctt ggt ctg ggc cgc ttc ttc agc tct 749
Gly Val Val Lys Leu Gly Asp Leu Gly Leu Gly Arg Phe Phe Ser Ser
185 190 195

gag acc acc gca gcc cac tcc cta gtg ggg acg ccc tac tac atg tca 797

Glu Thr Thr Ala Ala His Ser Leu Val Gly Thr Pro Tyr Tyr Met Ser

200 205 210 215

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ccg	gag	agg	atc	cat	gag	aac	ggc	tac	aac	ttc	aag	tcc	gac	atc	tgg	845
Pro	Glu	Arg	Ile	His	G1u	Asn	Gly	Tyr	Asn	Phe	Lys	Ser	Asp	Ile	Trp	
				220					225					230		
tcc	ttg	ggc	tgt	ctg	ctg	tac	gag	atg	gca	gcc	ctc	cag	agc	ccc	ttc	893
Ser	Leu	Gly	Cys	Leu	Leu	Tyr	Glu	Met	Ala	Ala	Leu	Gln	Ser	Pro	Phe	
			235					240					245			
tat	gga	gat	aag	atg	aat	ctc	ttc	tcc	ctg	tgc	cag	aag	atc	gag	cag	941
Tyr	Gly	Asp	Lys	Met	Asn	Leu	Phe	Ser	Leu	Cys	G1n	Lys	Ile	Glu	G1n	
		250					255					260				
tgt	gac	tac	ccc	cca	ctc	ccc	ggg	gag	cac	tac	tcc	gag	aag	tta	cga	989
Cys	Asp	Tyr	Pro	Pro	Leu	Pro	Gly	Glu	His	Tyr	Ser	Glu	Lys	Leu	Arg	
	265					270					275					
gaa	ctg	gtc	agc	atg	tgc	atc	tgc	cct	gac	ccc	cac	cag	aga	cct	gac	1037
G1u	Leu	Val	Ser	Met	Cys	Ile	Cys	Pro	Asp	Pro	His	Gln	Arg	Pro	Asp	
280					285					290					295	
atc	gga	tac	gtg	cac	cag	gtg	gcc	aag	cag	atg	cac	atc	tgg	atg	tcc	1085
Ile	Gly	Tyr	Val	His	Gln	Val	Ala	Lys	Gln	Met	His	Ile	Trp	Met	Ser	
				300					305					310		
agc	acc	tgag	cgt	gga t	gcac	cgtg	c ct	tato	aaag	g cca	agcac	cac	tttg	cctt	ac	1141
Ser	Thr															
ttga	agtce	rtc t	tctc	ettes	a gt	ggco	acct	get	agco	ctag	aaca	ageta	ag a	accac	agggt.	1201

111/735

teageaggtt ceceaaaagg etgeceagee ttacageaga tgetgaagge agageagetg 1261
agggagggge getggecaca tgteactgat ggteagatte caaagteett tetttataet 1321
gttgtggaca ateteagetg ggteaataag ggeaggtggt teagegagee aeggeageee 1381
cetgtatetg gattgtaatg tgaatettta gggtaattee teeagtgace tgteaagget 1441
tatgetaaca ggagaettge aggagaeegt gtgatttgtg tagtgageet ttgaaaatgg 1501
ttagtacegg gtteagttta gttettggta tettteaat caagetgtgt gettaattta 1561
ctetgttgta aagggataaa gtggaaatea tttttt

<210> 41

<211> 371

<212> PRT

<213> Homo sapiens

<400> 41

Met Ser His Glu Lys Ser Phe Leu Val Ser Gly Asp Asn Tyr Pro Pro

1 5 10 15

Pro Asn Pro Gly Tyr Pro Gly Gly Pro Gln Pro Pro Met Pro Pro Tyr
20 25 30

Ala Gln Pro Pro Tyr Pro Gly Ala Pro Tyr Pro Gln Pro Pro Phe Gln 112/735

WO 02/053737	PCT/JP01/11389

45

Pro Ser Pro Tyr Gly Gln Pro Gly Tyr Pro His Gly Pro Ser Pro Tyr
50 55 60

40

35

Pro Gln Gly Gly Tyr Pro Gln Gly Pro Tyr Pro Gln Gly Gly Tyr Pro 65 70 75 80

Gln Gly Pro Tyr Pro Gln Glu Gly Tyr Pro Gln Gly Pro Tyr Pro Gln
85 90 95

Gly Gly Tyr Pro Gln Gly Pro Tyr Pro Gln Ser Pro Phe Pro Pro Asn 100 105 110

Pro Tyr Gly Gln Pro Gln Val Phe Pro Gly Gln Asp Pro Asp Ser Pro 115 120 125

Gln His Gly Asn Tyr Gln Glu Glu Gly Pro Pro Ser Tyr Tyr Asp Asn 130 135 140

Gln Asp Phe Pro Ala Thr Asn Trp Asp Asp Lys Ser Ile Arg Gln Ala 145 150 155 160

Phe Ile Arg Lys Val Phe Leu Val Leu Thr Leu Gln Leu Ser Val Thr
165 170 175

Leu Ser Thr Val Ser Val Phe Thr Phe Val Ala Glu Val Lys Gly Phe
180 185 190

Val	Arg	G1u	Asn	Val	Trp	Thr	Tyr	Tyr	Val	Ser	Tyr	Ala	Val	Phe	Phe
		195					200					205			
T1.	C	I	T1.	V_1	T	C	Crro	Crra	C1	Aan	Dho	A ~~ ~	۸	Lvo	u; c
TIE		Leu	11e	Val	Leu		Cys	Cys	Gly	ASp		νιβ	vi R	rys	1112
	210					215					220				
Pro	Trp	Asn	Leu	Val	Ala	Leu	Ser	Val	Leu	Thr	Ala	Ser	Leu	Ser	Tyr
225					230					235					240
													,		
Ma+	V-1	C1	Ma+	T1.	410	Som	Dho	Ture.	Aan	Thr	Gl ₁₁	A1.a	Val	Tla	Mo+
Mer	vai	GIY	Mec		піа	261	rne	Tyr		1111	Giu	пта	Vai		Mec
				245					250					255	
Ala	Val	Gly	Ile	Thr	Thr	Ala	Val	Cys	Phe	Thr	Val	Val	Ile	Phe	Ser
			260					265					270		
Mot	G1n	Thr	Δra	Tur	Aen	Phe	Thr	Ser	Cvs	Met	G1 v	Va1	Ī.eu	Len	Val
Met	0111		111 6	1,1	пор	1110		501	0,0		01)		204	20.	
		275					280					285			
Ser	Met	Val	Val	Leu	Phe	Ile	Phe	Ala	Ile	Leu	Cys	Ile	Phe	Ile	Arg
	290					295					300				
Asn	Arg	Tle	Leu	Glu	Ile	Val	Tvr	Ala	Ser	Leu	Glv	Ala	Leu	Leu	Phe
	0					,					•				320
305					310					315					020
Thr	Cys	Phe	Leu	Ala	Val	Asp	Thr	Gln	Leu	Leu	Leu	Gly	Asn	Lys	G1n
				325					330					335	

Leu Ser Leu Ser Pro Glu Glu Tyr Val Phe Ala Ala Leu Asn Leu Tyr

340

345

114/735

350

Thr Asp Ile Ile Asn Ile Phe Leu Tyr Ile Leu Thr Ile Ile Gly Arg
355 360 365

Ala Lys Glu

370

<210> 42

<211> 1781

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (91).. (1203)

<400> 42

attggccatc accgcgcgc cgcgcagcgg acaccgtgcg taccggcctg cggcgcccgg 60

ccaccggggc ggaccgcgga acccgaggcc atg tcc cat gaa aag agt ttt ttg 114

Met Ser His Glu Lys Ser Phe Leu

1

5

gtg tct ggg gac aac tat cct ccc ccc aac cct gga tat ccg ggg ggg 162

Val Ser Gly Asp Asn Tyr Pro Pro Pro Asn Pro Gly Tyr Pro Gly Gly

10 15 20

ccc cag cca ccc atg ccc ccc tat gct cag cct ccc tac cct ggg gcc 210

Pro	Gln	Pro	Pro	Met	Pro	Pro	Tyr	Ala	Gln	Pro	Pro	Tyr	Pro	Gly	Ala	
25					30					35					40	
cct	tac	cca	cag	ссс	cct	ttc	cag	ссс	tcc	ссс	tac	ggt	cag	cca	ggg	258
Pro	Tyr	Pro	G1n	Pro	Pro	Phe	Gln	Pro	Ser	Pro	Tyr	Gly	Gln	Pro	Gly	
				45					50					55		
tac	ССС	cat	ggc	ссс	agc	ссс	tac	ссс	caa	ggg	ggc	tac	cca	cag	ggt	306
Гуŗ	Pro	His	Gly	Pro	Ser	Pro	Tyr	Pro	G1n	Gly	Gly	Tyr	Pro	Gln	Gly	
			60					65					70		·	
ccc	tac	ccc	caa	ggg	ggc	tac	cca	cag	ggc	ссс	tac	cca	caa	gag	ggc	354
Pro	Tyr	Pro	Gln	Gly	Gly	Tyr	Pro	Gln	Gly	Pro	Tyr	Pro	Gln	Glu	Gly	
		75					80					85				
tac	cca	cag	ggc	ссс	tac	ссс	caa	ggg	ggc	tac	ссс	cag	ggg	cca	tat	402
Tyr	Pro	Gln	Gly	Pro	Tyr	Pro	Gln	Gly	Gly	Tyr	Pro	Gln	Gly	Pro	Tyr	
	90					95					100					
ccc	cag	agc	ccc	ttc	ccc	ccc	aac	ccc	tat	gga	cag	cca	cag	gtc	ttc	450
Pro	Gln	Ser	Pro	Phe	Pro	Pro	Asn	Pro	Tyr	Gly	Gln	Pro	Gln	Val	Phe	
105					110					115					120	
cca	gga	caa	gac	cct	gac	tca	ccc	cag	cat	gga	aac	tac	cag	gag	gag	498
Pro	Gly	Gln	Asp	Pro	Asp	Ser	Pro	Gln	His	Gly	Asn	Tyr	Gln	Glu	Glu	
				125					130					135		
ggt	ccc	cca	tcc	tac	tat	gac	aac	cag	gac	ttc	cct	gcc	acc	aac	tgg	546
Gly	Pro	Pro	Ser	Tyr	Tyr	Asp	Asn			Phe	Pro	Ala	Thr	Asn	Trp	
								116	735							

			140					145					150			
gat	gac	aag	agc	atc	cga	cag	gcc	ttc	atc	cgc	aag	gtg	ttc	cta	gtg	594
_	_									Arg						
		155					160				•	165				
ctg	acc	ttg	cag	ctg	tcg	gtg	acc	ctg	tcc	acg	gtg	tct	gtg	ttc	act	642
Leu	Thr	Leu	Gln	Leu	Ser	Val	Thr	Leu	Ser	Thr	Val	Ser	Val	Phe	Thr	
	170					175					180					
ttt	gtt	gcg	gag	gtg	aag	ggc	ttt	gtc	cgg	gag	aat	gtc	tgg	acc	tac	690
Phe	Val	Ala	Glu	Val	Lys	Gly	Phe	Val	Arg	Glu	Asn	Val	Trp	Thr	Tyr	
185					190					195					200	
		•														
tat	gtc	tcc	tat	gct	gtc	ttc	ttc	atc	tct	ctc	atc	gtc	ctc	agc	tgt	738
Tyr	Val	Ser	Tyr	Ala	Val	Phe	Phe	Ile	Ser	Leu	Ile	Val	Leu	Ser	Cys	
				205					210					215		
tgt	ggg	gac	ttc	cgg	cga	aag	cac	ccc	tgg	aac	ctt	gtt	gca	ctg	tcg	786
Cys	Gly	Asp	Phe	Arg	Arg	Lys	His	Pro	Trp	Asn	Leu	Val	Ala	Leu	Ser	
			220					225					230			
gtc	ctg	acc	gcc	agc	ctg	tcg	tac	atg	gtg	ggg	atg	atc	gcc	agc	ttc	834
Val	Leu	Thr	Ala	Ser	Leu	Ser	Tyr	Met	Val	Gly	Met	Ile	Ala	Ser	Phe	
		235					240					245				
tac	aac	acc	gag	gca	gtc	atc	atg	gcc	gtg	ggc	atc	acc	aca	gcc	gtc	882
Tyr	Asn	Thr	Glu	Ala	Val	Ile	Met	Ala	Val	Gly	Ile	Thr	Thr	Ala	Val	

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255

250

260

tgc	ttc	acc	gtc	gtc	atc	ttc	tcc	atg	cag	acc	cgc	tac	gac	ttc	acc	930
Cys	Phe	Thr	Val	Val	Ile	Phe	Ser	Met	Gln	Thr	Arg	Tyr	Asp	Phe	Thr	
265					270					275					280	
tca	tgc	atg	ggc	gtg	ctc	ctg	gtg	agc	atg	gtg	gtg	ctc	ttc	atc	ttc	978
Ser	Cys	Met	Gly	Val	Leu	Leu	Val	Ser	Met	Val	Val	Leu	Phe	Ile	Phe	
				285					290					295		
gcc	att	ctc	tgc	atc	ttc	atc	cgg	aac	cgc	atc	ctg	gag	atc	gtg	tac	1026
Ala	Ile	Leu	Cys	Ile	Phe	Ile	Arg	Asn	Arg	Ile	Leu	Glu	Ile	Val	Tyr	
			300					305					310			
gcc	tca	ctg	ggc	gct	ctg	ctc	ttc	acc	tgc	ttc	ctc	gca	gtg	gac	acc	1074
Ala	Ser	Leu	Gly	Ala	Leu	Leu	Phe	Thr	Cys	Phe	Leu	Ala	Val	Asp	Thr	
		315					320					325				
cag	ctg	ctg	ctg	ggg	aac	aag	cag	ctg	tcc	ctg	agc	cca	gaa	gag	tat	1122
Gln	Leu	Leu	Leu	Gly	Asn	Lys	Gln	Leu	Ser	Leu	Ser	Pro	Glu	Glu	Tyr	
	330					335					340					
gtg	ttt	gct	gcg	ctg	aac	ctg	tac	aca	gac	atc	atc	aac	atc	ttc	ctg	1170
Val	Phe	Ala	Ala	Leu	Asn	Leu	Tyr	Thr	Asp	Ile	Ile	Asn	Ile	Phe	Leu	
345					350					355					360	
tac	atc	ctc	acc	atc	att	ggc	cgc	gcc	aag	gag	tago	ccga	gct	ccago	ctcgct	1223
Tyr	Ile	Leu	Thr	Ile	Ile	Gly	Arg	Ala	Lys	G1u						
				365					370							

gtgcccgctc aggtggcacg gctggcctgg accetgcccc tggcacggca gtgccagctg 1283

tacttcccct ctctcttgtc cccaggcaca gcctagggaa aaggatgcct ctctccaacc 1343

ctcctgtatg tacactgcag atacttccat ttggacccgc tgtggccaca gcatggcccc 1403

tttagtcctc ccgcccccgc caaggggcag caaggccacg tttccgtgcc acctcctgtc 1463

tactcattgt tgcatgagcc ctgtctgcca gcccacccca gggactgggg gcagcaccag 1523

gtcccgggga gagggattga gccaagaggt gagggtgcac gtcttccctc ctgtcccagc 1583

tccccagcct ggcgtagagc accectcccc tccccccac cccctggag tgctgccctc 1643

tggggacatg cggagtgggg gtcttatccc tgtgctgagc cctgagggca gagaggatgg 1703

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tgggatttgc tctctgcc

<210> 43

<211> 393

<212> PRT

<213> Homo sapiens

<400> 43

1

Met Ser Asp Glu Arg Glu Val Ala Glu Ala Ala Thr Gly Glu Asp Ala

10

15

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Ser	Ser	Pro	Pro 20	Pro	Lys	Thr	Glu	Ala 25	Ala	Ser	Asp	Pro	Gln 30	His	Pro
Ala	Ala	Ser 35	Glu	Gly	Ala	Ala	Ala 40	Ala	Ala	Ala	Ser	Pro 45	Pro	Leu	Leu
Arg	Cys 50	Leu	Val	Leu	Thr	Gly 55	Phe	Gly	Gly	Tyr	Asp 60	Lys	Val	Lys	Leu ·
G1n 65	Ser	Arg	Pro	Ala	Ala 70	Pro	Pro	Ala	Pro	Gly 75	Pro	G1y	G1n	Leu	Thr 80
Leu	Arg	Leu	Arg	Ala 85	Cys	G1y	Leu	Asn	Phe 90	Ala	Asp	Leu	Met	Ala 95	Arg
G1n	Gly	Leu	Tyr 100	Asp	Arg	Leu	Pro	Pro 105	Leu	Pro	Val	Thr	Pro 110	Gly	Met
Glu	Gly	Ala 115	Gly	Val	Val	Ile	Ala 120	Val	G1y	Glu	Gly	Val 125	Ser	Asp	Arg
Lys	Ala 130	Gly	Asp	Arg	Val	Met 135		Leu	Asn	Arg	Ser 140	Gly	Met	Trp	Gln
Glu 145	Glu	Val	Thr	Val	Pro 150	Ser	Val	Gln	Thr	Phe 155	Leu	Ile	Pro	G1u	Ala 160

Met Thr Phe Glu Glu Ala Ala Ala Leu Leu Val Asn Tyr Ile Thr Ala

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165 170 175

Tyr Met Val Leu Phe Asp Phe Gly Asn Leu Gln Pro Gly His Ser Val 180 185 190

Leu Val His Met Ala Ala Gly Gly Val Gly Met Ala Ala Val Gln Leu
195 200 205

Cys Arg Thr Val Glu Asn Val Thr Val Phe Gly Thr Ala Ser Ala Ser 210 215 220

Lys His Glu Ala Leu Lys Glu Asn Gly Val Thr His Pro Ile Asp Tyr 225 230 235 240

His Thr Thr Asp Tyr Val Asp Glu Ile Lys Lys Ile Ser Pro Lys Gly
245 250 255

Val Asp Ile Val Met Asp Pro Leu Gly Gly Ser Asp Thr Ala Lys Gly
260 265 270

Tyr Asn Leu Leu Lys Pro Met Gly Lys Val Val Thr Tyr Gly Met Ala 275 280 285

Asn Leu Leu Thr Gly Pro Lys Arg Asn Leu Met Ala Leu Ala Arg Thr
290 295 300

Trp Trp Asn Gln Phe Ser Val Thr Ala Leu Gln Leu Leu Gln Ala Asn 305 310 315 320

Arg Ala Val Cys Gly Phe His Leu Gly Tyr Leu Asp Gly Glu Val Glu 325 330 335

Leu Val Ser Gly Val Val Ala Arg Leu Leu Ala Leu Tyr Asn Gln Gly 340 345 350

His Ile Lys Pro His Ile Asp Ser Val Trp Pro Phe Glu Lys Val Ala 355 360 365

Asp Ala Met Lys Gln Met Gln Glu Lys Lys Asn Val Gly Lys Val Leu 370 375 380

Leu Val Pro Gly Pro Glu Lys Glu Asn 385 390

<210> 44

<211> 2396

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (50).. (1228)

<400> 44

agctgtgcac tctccatcca gctgtgcgct ctcgtcggga gtcccagcc atg tcc gac 58

Met Ser Asp

1

gag	aga	gag	gta	gcc	gag	gca	gcg	acc	ggg	gaa	gac	gcc	tct	tcg	ccg	106
Glu	Arg	G1u	Val	Ala	G1u	Ala	Ala	Thr	Gly	Glu	Asp	Ala	Ser	Ser	Pro	
	5					10					15					
v																
cct	ccg	aaa	acc	gag	gca	gcg	agc	gac	ccc	cag	cat	ccc	gcg	gcc	tcc	154
Pro	Pro	Lys	Thr	Glu	Ala	Ala	Ser	Asp	Pro	Gln	His	Pro	Ala	Ala	Ser	
20					25					30					35	•
gaa	ggg	gcc	gcc	gcc	gcc	gcc	gcc	tcg	ccg	cca	ctg	ctg	cgc	tgc	cta	202
Glu	Gly	Ala	Ala	Ala	Ala	Ala	Ala	Ser	Pro	Pro	Leu	Leu	Arg	Cys	Leu	
				40					45					50		
										gtg						250
Val	Leu	Thr		Phe	Gly	Gly	Tyr		Lys	Val	Lys	Leu		Ser	Arg	
			55					60					65			
																000
										cag						298
Pro	Ala		Pro	Pro	Ala	Pro		Pro	GIA	Gln	Leu		Leu	Arg	Leu	
		70					75					80				
000	acc	†#C		o to	220	++0	aca	asc	ctc	at a	act	aaa	020	aaa	cta	346
										atg Met						040
мg	85	Cys	Oly	Leu	non	90	AIG	пор	Leu	IIIC C	95	ME	OIII	Oly	Leu	
	00					50					50					
tac	gac	cgt.	ctc	CCE	cct	ctg	cct	gtc	act	ccg	ggc	atg	gag	ggc	gcg	394
										Pro						•
100	-	6			105				_	110	- •				115	

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ggt	gtt	gtg	atc	gca	gtg	ggc	gag	gga	gtc	agc	gac	cgc	aag	gca	gga	442
Gly	Val	Val	Ile	Ala	Val	Gly	Glu	Gly	Val	Ser	Asp	Arg	Lys	Ala	Gly	
				120					125					130	•	
gac	cgg	gtg	atg	gtg	ttg	aac	cgg	tca	ggg	atg	tgg	cag	gaa	gag	gtg	490
Asp	Arg	Val	Met	Val	Leu	Asn	Arg	Ser	Gly	Met	Trp	Gln	Glu	Glu	Val	
			135					140					145			
act	gtg	ccc	tcg	gtc	cag	acc	ttc	ctg	att	cct	gag	gcc	atg	acc	ttt	538
Thr	Val	Pro	Ser	Val	Gln	Thr	Phe	Leu	Ile	Pro	Glu	Ala	Met	Thr	Phe	
		150			•	-	155					160				
gag	gaa	gct	gct	gcc	ttg	ctc	gtc	aat	tac	att	aca	gcc	tac	atg	gtc	586
Glu	G1u	Ala	Ala	Ala	Leu	Leu	Val	Asn	Tyr	Ile	Thr	Ala	Tyr	Met	Val	
	165					170					175					
ctc	ttt	gac	ttc	ggc	aac	cta	cag	cct	ggc	cac	agc	gtc	ttg	gta	cac	634
Leu	Phe	Asp	Phe	Gly	Asn	Leu	G1n	Pro	Gly	His	Ser	Val	Leu	Val	His	
180					185					190					195	
atg	gct	gca	ggg	ggt	gtg	ggt	atg	gct	gcc	gtg	cag	ctg	tgc	cgt	aca	682
Met	Ala	Ala	Gly	Gly	Val	Gly	Met	Ala	Ala	Val	Gln	Leu	Cys	Arg	Thr	
				200					205					210		
gtg	gag	aat	gtg	aca	gtg	ttc	gga	acg	gcc	tcg	gcc	agc	aag	cac	gag	730
Val	Glu	Asn	Val	Thr	Val	Phe	Gly	Thr	Ala	Ser	Ala	Ser	Lys	His	Glu	
			215					220					225			
gca	ctg	aag	gag	aat	ggg	gtc	aca			atc	gac	tat	cac	acg	act	778
								124/	735							

Ala	Leu	Lys	Glu	Asn	Gly	Val	Thr	His	Pro	Ile	Asp	Tyr	His	Thr	Thr	
		230					235					240				
gac	tac	gtg	gat	gag	atc	aag	aag	att	tcc	cct	aaa	gga	gtg	gac	att	826
Asp	Tyr	Val	Asp	Glu	Ile	Lys	Lys	Ile	Ser	Pro	Lys	Gly	Val	Asp	Ile	
	245					250					255					
gtc	atg	gac	cct	ctg	ggt	ggg	tca	gat	act	gcc	aag	ggc	tac	aac	ctc	874
Val	Met	Asp	Pro	Leu	Gly	Gly	Ser	Asp	Thr	Ala	Lys	Gly	Tyr	Asn	Leu	
260					265					270					275	
ctg	aaa	ccc	atg	ggc	aaa	gtc	gtc	acc	tat	gga	atg	gcc	aac	ctg	ctg	922
Leu	Lys	Pro	Met	Gly	Lys	Val	Val	Thr	Tyr	Gly	Met	Ala	Asn	Leu	Leu	
				280					285					290		
acg	ggc	ccc	aaa	cgg	aac	ctg	atg	gcc	ctg	gcc	cgg	aca	tgg	tgg	aat	970
Thr	Gly	Pro	Lys	Arg	Asn	Leu	Met	Ala	Leu	Ala	Arg	Thr	Trp	Trp	Asn	
			295					300					305			
cag	ttc	agc	gtg	aca	gct	ctg	cag	ctg	ctg	cag	gcc	aac	cgg	gct	gtg	1018
Gln	Phe	Ser	Val	Thr	Ala	Leu	Gln	Leu	Leu	G1n	Ala	Asn	Arg	Ala	Val	
		310					315					320				
tgt	ggc	ttc	cac	ctg	ggc	tac	ctg	gat	ggt	gag	gtg	gag	ctg	gtc	agt	1066
Cys	Gly	Phe	His	Leu	Gly	Tyr	Leu	Asp	Gly	G1u	Val	Glu	Leu	Val	Ser	
	325					330					335					
ggt	gtg	gtg	gcc	cgc	ctc	ctg	gct	ctg	tac	aac	cag	ggc	cac	atc	aag	1114
Gly	Val	Val	Ala	Arg	Leu	Leu	Ala			Asn	Gln	Gly	His	Ile	Lys	
						;		125	/735							

340	345	350	355
ccc cac att gac tca	gtc tgg ccc ttc ga	g aag gtg gct gat	t gcc atg 1162
Pro His Ile Asp Ser	Val Trp Pro Phe Gl	ı Lys Val Ala Ası	Ala Met
360	36	5	370
aaa cag atg cag gag	aag aag aat gtg gg	c aag gtc ctc ctg	g gtt cca 1210
Lys Gln Met Gln Glu	Lys Lys Asn Val Gl	y Lys Val Leu Lei	ı Val Pro
375	380	385	
0.0			•
			1050
ggg cca gag aag gag		tgtgaga ccctagaga	ac 1258
Gly Pro Glu Lys Glu	Asn		
390			
cagcgaaggg agaagttgg	gg aagctacgtt ctgtt	ggcca ccagacttgc	atttcagcct 1318
ctgtcataat gctctgcco	t ccctcccccg aagtt	ctctg tggtgatgac	cgctctcccc 1378
	5 5		
*		~~~~ +~~~~~++~	got at ot aga 1439
tgcccctccc cgcttcctg	ga ccicigaaga ggiig	ggaag tgaccattig	gatgictiggg 1450
ccctgccaag gcgacaggg	ga gggtcagagg gaggc	egget getteetgee	cccacccttt 1498
	•		
ccccgggcct gctgtgctg	c ttttgtgcca aggtt	agcca gtccccctg	ttgtgttcca 1558
tgtgctttca cctctgcct	c atctttcctc ccgtc	cctgc cccgccacct	ccccaaagaa 1618
- -	· ·		
ttgaaacgtc agctcagga	at atggggggg totot	otogo tecadestat	acctotetet 1679
vigaaaugio agovoagga	·· ulggggulaa illili	stoup totageauge	TOO DE COUCE TO 10

ccctagtgtc ccttcagcct gggctgacca gtgcccgcct ctgggcttga ccagttccca 1738 126/735

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atctcgtcct ctgtccccaa cttcttaagc acaattgggc ttcttccatc tccaggtttt 1798 ctgccattct taaccaaggc agccccaagc ctcctgggga ggcagggcaa aaacaggtgc 1858 cctcatcgtg gtctgtgcca tgtcccgtct ctatggtggt tgaggagaaa ggcggggaag 1918 cttcctcagc cttgcagata tgtgtggcat ttactagcca gagctctgaa aggcagtgct 1978 gtctgtttct tgtactggga ccaaagtaaa aatccaagca cattcccctt gcagttaggg 2038 gaggecetae tgeettetea aageagagag geagettate aaacteagee caaaactetg 2098 tttacatggg tggggagatg gagcagggaa gtacagagtg ggatggtcag gacctgggcc 2158 attgcaacca aaatggggac ttcctgggta gggaggtcac tccctctact cactgagcta 2218 ggattaggga gggttattgc cccaaccatt gcaatgggag gtggagggac aggctcagcc 2278 tcctcattgt ctaaatgagg cctaaatgtg tgaagtgcga tttctgcttt tgtgtacccc 2338 accaccccat taccacagct gcctttgtgt gtttgtgtca ataaaaagcc aaaccctg 2396

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<211> 393

<212> PRT

<213> Homo sapiens

<400> 45

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Ser Ser Pro Pro Pro Lys Thr Glu Ala Ala Ser Asp Pro Gln His Pro
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Ala Ala Ser Glu Gly Ala Ala Ala Ala Ala Ser Pro Pro Leu Leu
35 40 45

Arg Cys Leu Val Leu Thr Gly Phe Gly Gly Tyr Asp Lys Val Lys Leu 50 55 60

Gln Ser Arg Pro Ala Ala Pro Pro Ala Pro Gly Pro Gly Gln Leu Thr
65 70 75 80

Leu Arg Leu Arg Ala Cys Gly Leu Asn Phe Ala Asp Leu Met Ala Arg

85 90 95

Gln Gly Leu Tyr Asp Arg Leu Pro Pro Leu Pro Val Thr Pro Gly Met 100 105 110

Glu Gly Ala Gly Val Val Ile Ala Val Gly Glu Gly Val Ser Asp Arg 115 120 125

Lys Ala Gly Asp Arg Val Met Val Leu Asn Arg Ser Gly Met Trp Gln 130 135 140

Glu Glu Val Thr Val Pro Ser Val Gln Thr Phe Leu Ile Pro Glu Ala 128/735

145					150					155					160
Met	Thr	Phe	Glu	Glu 165	Ala	Ala	Ala	Leu	Leu 170	Val	Asn	Tyr	Ile	Thr 175	Ala
Tyr	Met	Val	Leu 180	Phe	Asp	Phe	Gly	Asn 185	Leu	G1n	Pro	Gly	His 190	Ser	Val
Leu	Val	His 195	Met	Ala	Ala	Gly	Gly 200	Val	Gly	Met	Ala	Ala 205	Val	Gln	Leu
Cys	Arg 210	Thr	Val	Glu	Asn	Val 215	Thr	Val	Phe	G1y	Thr 220	Ala	Ser	Ala	Ser
Lys 225	His	Glu	Ala	Leu	Lys 230	Glu	Asn	G1y	Val	Thr 235	His	Pro	Ile	Asp	Tyr 240
His	Thr	Thr	Asp	Tyr 245	Val	Asp	Glu	Ile	Lys 250	Lys	Ile	Ser	Pro	Lys 255	Gly
Val	Asp	Ile	Val 260	Met	Asp	Pro	Leu	Gly 265	Gly	Ser	Asp	Thr	Ala 270	Lys	Gly
Tyr	Asn	Leu 275	Leu	Lys	Pro	Met	Gly 280	Lys	Val	Val	Thr	Tyr 285	Gly	Met	Ala
Asn	Leu	Leu	Thr	Gly	Pro	Lys	Arg	Asn	Leu	Met	Ala	Leu	Ala	Arg	Thr

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300

295

290

Trp Trp Asn Gln Phe Ser Val Thr Ala Leu Gln Leu Leu Gln Ala Asn 305 310 315 320

Arg Ala Val Cys Gly Phe His Leu Gly Tyr Leu Asp Gly Glu Val Glu
325 330 335

Leu Val Ser Gly Val Val Ala Arg Leu Leu Ala Leu Tyr Asn Gln Gly
340 345 350

His Ile Lys Pro His Ile Asp Ser Val Trp Pro Phe Glu Lys Val Ala 355 360 365

Asp Ala Met Lys Gln Met Gln Glu Lys Lys Asn Val Gly Lys Val Leu 370 375 380

Leu Val Pro Gly Pro Glu Lys Gln Asn 385 390

<210> 46

<211> 2396

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (50).. (1228)

<400> 46

130/735

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													Me	et Se	er Asp	
														1		
gag	aga	gag	gta	gcc	gag	gca	gcg	acc	ggg	gaa	gac	gcc	tct	tcg	ccg	106
Glu	Arg	Glu	Val	Ala	Glu	Ala	Ala	Thr	Gly	Glu	Asp	Ala	Ser	Ser	Pro	
	5					10					15					
cct	ccg	aaa	acc	gag	gca	gcg	agc	gac	ccc	cag	cat	ccc	gcg	gcc	tcc	154
Pro	Pro	Lys	Thr	Glu	Ala	Ala	Ser	Asp	Pro	Gln	His	Pro	Ala	Ala	Ser	
20					25					30					35	
gaa	ggg	gcc	gcc	gcc	gcc	gcc	gcc	tcg	ccg	cca	ctg	ctg	cgc	tgc	cta	202
Glu	Gly	Ala	Ala	Ala	Ala	Ala	Ala	Ser	Pro	Pro	Leu	Leu	Arg	Cys	Leu	
				40					45					50		
								•								
gtg	ctc	acc	ggc	ttt	gga	ggc	tac	gac	aag	gtg	aag	ctg	cag	agc	cgg	250
														Ser		
			55		·		_	60					65			
ccg	gca	gcg	ccc	ccg	gcc	cct	ggg	ccc	ggc	cag	ctg	acg	ctg	cgt	ctg	298

Pro Ala Ala Pro Pro Ala Pro Gly Pro Gly Gln Leu Thr Leu Arg Leu
70 75 80

cgg gcc tgc ggg ctc aac ttc gca gac ctc atg gct agg cag ggg ctg 346
Arg Ala Cys Gly Leu Asn Phe Ala Asp Leu Met Ala Arg Gln Gly Leu
85 90 95

tac gac cgt ctc ccg cct ctg cct gtc act ccg ggc atg gag ggc gcg 394 131/735

Tyr	Asp	Arg	Leu	Pro	Pro	Leu	Pro	Val	Thr	Pro	Gly	Met	Glu	Gly	Ala	
100					105					110					115	
ggt	gtt	gtg	atc	gca	gtg	ggc	gag	gga	gtc	agc	gac	cgc	aag	gca	gga	442
Gly	Val	Val	Ile	Ala	Val	Gly	Glu	Gly	Val	Ser	Asp	Arg	Lys	Ala	Gly	
				120					125					130		
gac	cgg	gtg	atg	gtg	ttg	aac	cgg	tca	ggg	atg	tgg	cag	gaa	gag	gtg	490
Asp	Arg	Val	Met	Val	Leu	Asn	Arg	Ser	G1y	Met	Trp	Gln	G1u	Glu	Va1	
			135					140					145			
act	gtg	ccc	tcg	gtc	cag	acc	ttc	ctg	att	cct	gag	gcc	atg	acc	ttt	538
Thr	Val	Pro	Ser	Val	Gln	Thr	Phe	Leu	Ile	Pro	Glu	Ala	Met	Thr	Phe	
		150					155					160				
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gag	gaa	gct	gct	gcc	ttg	ctc	gtc	aat	tac	att	aca	gcc	tac	atg	gtc	586
Glu	G1u	Ala	Ala	Ala	Leu	Leu	Val	Asn	Tyr	Ile	Thr	Ala	Tyr	Met	Val	
	165					170					175					
ctc	ttt	gac	ttc	ggc	aac	cta	cag	cct	ggc	cac	agc	gtc	ttg	gta	cac	634
						Leu							_			
180		-		•	185					190					195	
ate	gct	gca	222	ggt	gtg	ggt	ate	gct	gcc	gtg	cag	ctg	tgc	cgt	aca	682
						Gly										
inc c	1110	7110	01)	200		01,	11100	1114	205	, 42	-		-,-	210		
				200					200							
a+~	ae a	20+	a+~	aca	art ar	++^	a.c.o	207	acc.	tea	acc	age	990	cac		720
																130
val	GIU	ASII	AST	THE	val	rue	ΩŢΆ	132/		Set	VIS	OGI.	гàд	1112	JIU	
						ttc Phe		Thr	Ala							730

			215					220					225			
gca	ctg	aag	gag	aat	ggg	gtc	aca	cat	ccc	atc	gac	tat	cac	acg	act	778
Ala	Leu	Lys	Glu	Asn	Gly	Val	Thr	His	Pro	Ile	Asp	Tyr	His	Thr	Thr	
		230					235					240				
gac	tac	gtg	gat	gag	atc	aag	aag	att	tcc	cct	aaa	gga	gtg	gac	att	826
Asp	Tyr	Val	Asp	Glu	Ile	Lys	Lys	Ile	Ser	Pro	Lys	Gly	Val	Asp	Ile	
	245					250					255					
gtc	atg	gac	cct	ctg	ggt	ggg	tca	gat	act	gcc	aag	ggc	tac	aac	ctc	874
	Met												_		_	
260		-			265	•		-		270					275	
ctg	aaa	ссс	atg	ggc	aaa	gtc	gtc	acc	tat	gga	atg	gcc	aac	ctg	ctg	922
Leu	Lys	Pro	Met	Gly	Lys	Val	Val	Thr	Tyr	Gly	Met	Ala	Asn	Leu	Leu	
				280					285					290		
	ggc															970
Thr	Gly	Pro	Lys	Arg	Asn	Leu	Met		Leu	Ala	Arg	Thr	Trp	Trp	Asn	
			295					300					305			
Cag	ttc	agc	ete	aca	gct	ctg	cag	cte	ctg	cag	gcc	aac	CZZ	gct	gtg	1018
_	Phe	_			_											
OIII	The	310	741	1111	MIG	Dou	315	Dou	Dou	OIII		320	1116	7114	, 41	
		310					010					020				
tgt	ggc	ttc	cac	ctg	ggc	tac	ctg	gat	ggt	gag	gtg	gag	ctg	gtc	agt	1066
Cys	Gly	Phe	His	Leu	G1y	Tyr	Leu	Asp	Gly	Glu	Val	G1u	Leu	Val	Ser	
	325					330					335					
								133/	735							

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ggt	gtg	gtg	gcc	cgc	ctc	ctg	gct	ctg	tac	aac	cag	ggc	cac	atc	aag	1114
Gly	Val	Val	Ala	Arg	Leu	Leu	Ala	Leu	Tyr	Asn	G1n	Gly	His	Ile	Lys	
340					345					350					355	

ccc cac att gac tca gtc tgg ccc ttc gag aag gtg gct gat gcc atg 1162
Pro His Ile Asp Ser Val Trp Pro Phe Glu Lys Val Ala Asp Ala Met
360 365 370

aaa cag atg cag gag aag aag aat gtg ggc aag gtc ctc ctg gtt cca 1210 Lys Gln Met Gln Glu Lys Lys Asn Val Gly Lys Val Leu Leu Val Pro 375 380 385

ggg cca gag aag cag aac tagggcaagt ggctgtgaga ccctagagac 1258 Gly Pro Glu Lys Gln Asn

390

cagcgaaggg agaagttggg aagctacgtt ctgttggcca ccagacttge atttcagcct 1318
ctgtcataat gctctgccct ccctccccg aagttctctg tggtgatgac cgctctccc 1378
tgcccctccc cgcttcctga cctctgaaga ggttgggaag tgaccatttg gatgtctggg 1438
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<210> 47

<211> 138

<212> PRT

<213> Homo sapiens

⟨400⟩ 47

Met Ile Ser Leu Thr Asp Thr Gln Lys Ile Gly Met Gly Leu Thr Gly

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Phe Gly Val Phe Phe Leu Phe Phe Gly Met Ile Leu Phe Phe Asp Lys
20 25 30

Ala Leu Leu Ala Ile Gly Asn Val Leu Phe Val Ala Gly Leu Ala Phe
35 40 45

Val Ile Gly Leu Glu Arg Thr Phe Arg Phe Phe Gln Lys His Lys
50 55 60

Met Lys Ala Thr Gly Phe Phe Leu Gly Gly Val Phe Val Val Leu Ile
65 70 75 80

Gly Trp Pro Leu Ile Gly Met Ile Phe Glu Ile Tyr Gly Phe Phe Leu

85 90 95

Leu Phe Arg Gly Phe Phe Pro Val Val Val Gly Phe Ile Arg Arg Val
100 105 110

Pro Val Leu Gly Ser Leu Leu Asn Leu Pro Gly Ile Arg Ser Phe Val 115 120 125

Asp Lys Val Gly Glu Ser Asn Asn Met Val 136/735

135 130

<210> 48

<211> 2976

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (110).. (523)

<400> 48

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accetggget tteegaggtg etgtegeege tgteeceace actgeagee atg ate tee 118 Met Ile Ser

1

tta acg gac acg cag aaa att gga atg gga tta aca gga ttt gga gtg 166 Leu Thr Asp Thr Gln Lys Ile Gly Met Gly Leu Thr Gly Phe Gly Val 10 15

ttt ttc ctg ttc ttt gga atg att ctc ttt ttt gac aaa gca cta ctg 214 Phe Phe Leu Phe Phe Gly Met Ile Leu Phe Phe Asp Lys Ala Leu Leu 30 35 20 25

gct att gga aat gtt tta ttt gta gcc ggc ttg gct ttt gta att ggt 262 Ala Ile Gly Asn Val Leu Phe Val Ala Gly Leu Ala Phe Val Ile Gly 137/735

				40					45					50		
tta	gaa	aga	aca	ttc	aga	ttc	ttc	ttc	caa	aaa	cat	aaa	atg	aaa	gct	310
Leu	Glu	Arg	Thr	Phe	Arg	Phe	Phe	Phe	Gln	Lys	His	Lys	Met	Lys	Ala	
			55					60					65			
aca	ggt	ttt	ttt	ctg	ggt	ggt	gta	ttt	gta	gtc	ctt	att	ggt	tgg	cct	358
Thr	Gly	Phe	Phe	Leu	Gly	Gly	Val	Phe	Val	Val	Leu	Ile	Gly	Trp	Pro	
		70					75					80				
ttg	ata	ggc	atg	atc	ttc	gaa	att	tat	gga	ttt	ttt	ctc	ttg	ttc	agg	406
_								Tyr							-, -	
	85	,				90		- , -	,		95					
	00															
	**-		+			_++			-44			_4_				454
								ttt								454
	Phe	Phe	Pro	Val	Val	Val	GLy	Phe	lle	Arg	Arg	Val	Pro	Val		
100					105					110					115	
gga	tcc	ctc	cta	aat	tta	cct	gga	att	aga	tca	ttt	gta	gat	aaa	gtt	502
Gly	Ser	Leu	Leu	Asn	Leu	Pro	Gly	Ile	Arg	Ser	Phe	Val	Asp	Lys	Val	
				120					125					130		
gga	gaa	agc	aac	aat	atg	gta	taad	caaca	aag 1	gaat	ttga	aa ga	actca	ittta	ı	553
Gly	Glu	Ser	Asn	Asn	Met	Val										
-			135													

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aaatagcttg taatgttctt tacaggagtt taaaacgtat agcctacaaa gtaccagcag 673 138/735

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taaaaggtta aacttatggc tgtttttaaa gggctattca tttaatctga gttttccctt 1573 attttcagct ttttcctagc atataatagt cattaagcat gacatatcct tcatatgatc 1633 actcatcttg agttaattag aaaatacctg agttcacgtg ctaaagtcat ttcactgtaa 1693 taaactgact atggtttctt aagaacatga cactaaaaaa aaagtggttt ttttccaccg 1753 ttgctgatta ttagacagta ggaaatagct gttttcttta gttttacaag atgtgacagc 1813 tttagtggta gatgtaggga aacatttcaa cagccatagt actatttgtt ttaccactga 1873 ttgcactgtt ttgtttttt aacagttgca aagcttttta atgcataaaa gtataattga 1933 tagttaaatc tettaataca cagagaactc ccaatcttgc tcatctaaat aaggaaagac 2053 ttggtgtata gtgtgatggt ttagtcttaa ggattaagac atttttggta cttgcatttg 2113 acttacgatg tatctgtgaa aatgggatga tattgacaaa tggagactcc tacctcaata 2173 gttaatggaa taataagagg ctactgttgt gtctaatgtt cttcaaaaaa gtaatatcct 2233 cacttggaga gtgtcaaata catactttga ggattgactt tatataaggt gccctgtaga 2293 actetgttae acatattttt gacceatatt atttacaatg tettgataat tetacetttt 2353 tagagcaaga atagtatctg ctaatgtaag ggacatctgt atttaactcc tttgtagaca 2413 140/735

tgaattteta teaaaatgtt etttgeactg taacagagat teettttte aataatetta 2473
atteaaaage attattagae ttgaaagggt ttgataatet eecagteett agtaaagatt 2533
gagagagget ggageagttt teagtttaa atgagtetge agttaatate aaatgtgagt 2593
ttgggaetge etggeaacat ttatatteet tatteagaae eettgatgag aetatttta 2653
aacatactag tetgetgata gaaageacta tacateetat tgtttette ttteeaaaat 2713
cageettetg tetgtaacaa aaatgtaett tatagagatg gaggaaaagg tetaataeta 2773
catageetta agtgttetg teattgtea agtgtattt etgtaacaga aacatatttg 2833
gaatgtttt ettteeeet tataaattgt aatteetgaa ataetgetge tttaaaaagg 2893
ceeactgtea gattatatta tetaacaatt gaatattgta aataaettg tettaeeete 2953
caataaaaagg gtaettteet att

<210> 49

<211> 359

<212> PRT

<213> Homo sapiens

<400> 49

Met Ser Lys Glu Thr Ile Ile Lys Cys Glu Lys Gln Lys Pro Arg Phe 141/735

1 5 10 15

His Ala Phe Leu Lys Ile Asn Gln Ala Lys Pro Glu Cys Gly Arg Gln
20 25 30

Ser Leu Val Glu Leu Leu Ile Arg Pro Val Gln Arg Leu Pro Ser Val
35 40 45

Ala Leu Leu Leu Asn Asp Leu Lys Lys His Thr Ala Asp Glu Asn Pro
50 55 60

Asp Lys Ser Thr Leu Glu Lys Ala IIe Gly Ser Leu Lys Glu Val Met
65 70 75 80

Thr His Ile Asn Glu Asp Lys Arg Lys Thr Glu Ala Gln Lys Gln Ile

85 90 95

Phe Asp Val Val Tyr Glu Val Asp Gly Cys Pro Ala Asn Leu Leu Ser 100 105 110

Ser His Arg Ser Leu Val Gln Arg Val Glu Thr Ile Ser Leu Gly Glu 115 120 125

His Pro Cys Asp Arg Gly Glu Gln Val Thr Leu Phe Leu Phe Asn Asp 130 135 140

Cys Leu Glu Ile Ala Arg Lys Arg His Lys Val Ile Gly Thr Phe Arg 145 150 155 160

Ser	Pro	His	Gly	Gln	Thr	Arg	Pro	Pro	Ala	Ser	Leu	Lys	His	Ile	His
				165					170					175	
Leu	Met	Pro	Leu	Ser	Gln	Ile	Lys	Lys	Val	Leu	Asp	Ile	Arg	Glu	Thr
			180					185					190		
Glu	Asp	Cys	His	Asn	Ala	Phe	Ala	Leu	Leu	Val	Arg	Pro	Pro	Thr	Glu
		195					200					205			
G1n	Ala	Asn	Val	Leu	Leu	Ser	Phe	Gln	Met	Thr	Ser	Asp	Glu	Leu	Pro
	210					215					220				
			-												
Lys	G1u	Asn	Trp	Leu	Lys	Met	Leu	Cys	Arg	His	Val	Ala	Asn	Thr	Ile
225					230					235					240

Cys Lys Ala Asp Ala Glu Asn Leu Ile Tyr Thr Ala Asp Pro Glu Ser 245 250 255

Phe Glu Val Asn Thr Lys Asp Met Asp Ser Thr Leu Ser Arg Ala Ser
260 265 270

Arg Ala Ile Lys Lys Thr Ser Lys Lys Val Thr Arg Ala Phe Ser Phe 275 280 285

Ser Lys Thr Pro Lys Arg Ala Leu Arg Arg Ala Leu Met Thr Ser His 290 295 300

Gly Ser Val Glu Gly Arg Ser Pro Ser Ser Asn Asp Lys His Val Met
305 310 315 320
143/735

Ser Arg Leu Ser Ser Thr Ser Ser Leu Ala Gly Ile Pro Ser Pro Ser 325 330 335

Leu Val Ser Leu Pro Ser Phe Phe Glu Arg Arg Ser His Thr Leu Ser 340 345 350

Arg Ser Thr Thr His Leu Ile 355

<210> 50

<211> 2636

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (327).. (1403)

<400> 50

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atgttaatat attggcaaca attattcagt tatttcaagt accattggaa gaggaaggac 120
aacgtggtgg acctatcctt gcaccagagg agattaagac tatttttggt agcatcccag 180

144/735

atatctttga tgtacacact aagataaagg atgatcttga agaccttata gttaattggg 240

atg	agago	caa	aagc	attg	gt ga	acat [.]	tttt	c tg	aaat	attc	aaa	agat	ttg	gtaa	aaacct	300
acc	ctcc	ctt	tgta	aact [.]	tc t	ttga		_		_					a tgt	353
							Me	t Se	r Ly:	s Gl	u Th:	r Il	e Il	e Ly:	s Cys	
								1			ļ	5				
gaa	aaa	cag	aaa	cca	aga	ttt	cat	gct	ttt	ctc	aag	ata	aac	caa	gca	401
Glu	Lys	Gln	Lys	Pro	Arg	Phe	His	Ala	Phe	Leu	Lys	Ile	Asn	Gln	Ala	
10					15					20					25	
ааа	cca	gaa	t.gt	gga	Cgg	cag	agc	ctt	gt.t.	gaa	ctt	ctt	atc	cga	cca	449
														Arg		
2,3	110	014	0,0	30	,,,,	O,III	DUL	Dou	35	Olu	Dou	Dou	110	40	110	
				30					30					40		
gta	cag	agg	tta	ccc	agt	gtt	gca	tta	ctt	tta	aat	gat	ctt	aag	aag	497
Val	Gln	Arg	Leu	Pro	Ser	Val	Ala	Leu	Leu	Leu	Asn	Asp	Leu	Lys	Lys	
			45					50					55			
cat	aca	gct	gat	gaa	aat	сса	gac	aaa	agc	act	tta	gaa	aaa	gct	att	545
His	Thr	Ala	Asp	Glu	Asn	Pro	Asp	Lys	Ser	Thr	Leu	Glu	Lys	Ala	Ile	
		60					65					70		•		
gga	tca	ctg	aag	gaa	gta	atg	acg	cat	att	aat	gag	gat	aag	aga	aaa	593
Gly	Ser	Leu	Lys	Glu	Val	Met	Thr	His	Ile	Asn	Glu	Asp	Lys	Arg	Lys	
	75					80					85					
aca	gaa	gct	caa	aag	caa	att	ttt	gat	gtt	gtt	tat	gaa	gta	gat	gga	641
				_										Asp		
				_				-						-		

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tgc	cca	gct	aat	ctt	tta	tct	tct	cac	cga	agc	tta	gta	cag	cgg	gtt	689
Cys	Pro	Ala	Asn	Leu	Leu	Ser	Ser	His	Arg	Ser	Leu	Val	Gln	Arg	Val	
				110					115					120		
																707
									tgt							737
Glu	Thr	Ile		Leu	Gly	Glu	His		Cys	Asp	Arg	Gly		GIn	Val	
			125					130					135			
act	ctc	ttc	ctc	ttc	aat	gat	tgc	cta	gag	ata	gca	aga	aaa	cgg	cac	785
									Glu							
		140				_	145					150				
aag	gtt	att	ggc	act	ttt	agg	agt	cct	cat	ggc	caa	acc	cga	ссс	cca	833
Lys	Val	Ile	G1y	Thr	Phe	Arg	Ser	Pro	His	Gly	G1n	Thr	Arg	Pro	Pro	
	155					160					165					
gct	tct	ctt	aag	cat	att	cac	cta	atg	cct	ctt	tct	cag	att	aag	aag	881
Ala	Ser	Leu	Lys	His	Ile	His	Leu	Met	Pro	Leu	Ser	Gln	Ile	Lys	Lys	
170					175					180					185	
gta	ttg	gac	ata	aga	gag	aca	gaa	gat	tgc	cat	aat	gct	ttt	gcc	ttg	929
Val	Leu	Asp	Ile	Arg	Glu	Thr	Glu	Asp	Cys	His	Asn	Ala	Phe	Ala	Leu	
				190					195					200		
ctt	gtg	agg	cca	cca	aca	gag	cag	gca	aat	gtg	cta	ctc	agt	ttc	cag	977
Leu	Val	Arg	Pro	Pro	Thr	Glu	G1n	Ala	Asn	Val	Leu	Leu	Ser	Phe	G1n	
			205					210					215			

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atg	aca	tca	gat	gaa	ctt	cca	aaa	gaa	aac	tgg	cta	aag	atg	ctg	tgt	1025
Met	Thr	Ser	Asp	Glu	Leu	Pro	Lys	Glu	Asn	Trp	Leu	Lys	Met	Leu	Cys	
		220					225					230				
cga	cat	gta	gct	aac	acc	att	tgt	aaa	gca	gat	gct	gag	aat	ctt	att	1073
Arg	His	Val	Ala	Asn	Thr	Ile	Cys	Lys	Ala	Asp	Ala	Glu	Asn	Leu	Ile	
	235					240					245					
tat	act	gct	gat	cca	gaa	tcc	ttt	gaa	gta	aat	aca	aaa	gat	atg	gac	1121
Tyr	Thr	Ala	Asp	Pro	Glu	Ser	Phe	Glu	Val	Asn	Thr	Lys	Asp	Met	Asp	
250					255					260					265	
agt	aca	ttg	agt	aga	gca	tca	aga	gca	ata	aaa	aag	act	tca	aaa	aag	1169
Ser	Thr	Leu	Ser	Arg	Ala	Ser	Arg	Ala	Ile	Lys	Lys	Thr	Ser	Lys	Lys	
				270					275					280		
gtt	aca	aga	gca	ttc	tct	ttc	tcc	aaa	act	cca	aaa	aga	gct	ctt	cga	1217
Val	Thr	Arg	Ala	Phe	Ser	Phe	Ser	Lys	Thr	Pro	Lys	Arg	Ala	Leu	Arg	
			285					290					295			
agg	gct	ctt	atg	aca	tcc	cac	ggc	tca	gtg	gag	gga	aga	agt	cct	tcc	1265
Arg	Ala	Leu	Met	Thr	Ser	His	G1y	Ser	Val	G1u	Gly	Arg	Ser	Pro	Ser	
		300					305					310				
agc	aat	gat	aag	cat	gta	atg	agt	cgt	ctt	tct	agc	aca	tca	tca	tta	1313
Ser	Asn	Asp	Lys	His	Val	Met	Ser	Arg	Leu	Ser	Ser	Thr	Ser	Ser	Leu	
	315					320					325					
						-										
gca	ggt.	atc	cct	tet	ccc	tee	ctt	gtc	agc	ctt	cct	too	tte	ttt	gaa	1361
3-4	00 °							147/					300	200	ouu	1001

Ala Gly Ile Pro Ser Pro Ser Leu Val Ser Leu Pro Ser Phe Phe Glu 330 335 340 345

agg aga agt cat acg tta agt aga tct aca act cat ttg ata

1403

Arg Arg Ser His Thr Leu Ser Arg Ser Thr Thr His Leu Ile

350

355

tgaagcgtta ccaaaatctt aaattataga aatgtataga cacctcatac tcaaataaga 1463 aactgactta aatggtactt gtaattagca cttggtgaaa gctggaagga agataaataa 1523 cactaaacta tgctatttga tttttcttct tgaaagagta aggtttacct gttacatttt 1583 caagttaatt catgtaaaaa atgatagtga ttttgatgta atttatctct tgtttgaatc 1643 tgtcattcaa aggccaataa tttaagttgc tatcagctga tattagtagc tttgcaaccc 1703 tgatagagta aataaatttt atgggcgggt gccaaatact gctgtgaatc tatttgtata 1763 gtatccatga atgaatttat ggaaatagat atttgtgcag ctcaatttat gcagagatta 1823 aatgacatca taatactgga tgaaaacttg catagaattc tgattaaata gtgggtctgt 1883 ttcacatgtg cagtttgaag tatttaaata accactcctt tcacagttta ttttcttctc 1943 aagcgttttc aagatctagc atgtggattt taaaagattt gccctcatta acaagaataa 2003 catttaaagg agattgtttc aaaatatttt tgcaaattga gataaggaca gaaagattga 2063

gaaacattgt atattttgca aaaacaagat gtttgtagct gtttcagaga gagtacggta 2123

tatttatggt aattttatcc actagcaaat cttgatttag tttgatagtg tgtggaattt 2183

tattttgaag gataagacca tgggaaaatt gtggtaaaga ctgtttgtac ccttcatgaa 2243

ataattctga agttgccatc agttttacta atcttctgtg aaatgcatag atatgcgcat 2303

gttcaacttt ttattgtggt cttataatta aatgtaaaat tgaaaattca tttgctgttt 2363

caaagtgtga tatcttcac aatagccttt ttatagtcag taattcagaa taatcaagtt 2423

catatggata aatgcattt tatttcctat ttctttaggg agtgctacaa atgtttgtca 2483

cttaaatttc aagttctgt tttaatagtt aactgactat agattgttt ctatgccatg 2543

tatgtgccac ttctgagagt agtaaatgac tctttgctac attttaaaag caattgtatt 2603

agtaagaact ttgtaaataa atacctaaaa ccc 2636

<210> 51

<211> 883

<212> PRT

<213> Homo sapiens

<400> 51

Met Ala Glu Asn Ser Val Leu Thr Ser Thr Thr Gly Arg Thr Ser Leu

1 5 10 15 149/735

Ala	Asp	Ser	Ser	Ile	Phe	Asp	Ser	Lys	Val	Thr	G1u	Ile	Ser	Lys	Glu
			20					25					30		
Asn	Leu	Leu	Ile	Gly	Ser	Thr	Ser	Tyr	Val	Glu	Glu	G1u	Met	Pro	G1n
		35					40					45			
~ 1	01	mı.		,, ,	71	v	1	0.1	01		01		01	01	0.3
Ile		Ihr	Arg	vaı	11e		Val	GIn	GIU	Ата		Lys	GIn	Glu	Glu
	50					55					60				
Leu	Thr	Lvs	Ala	Leu	ī.vs	Asp	Tle	Lvs	Va1	G] v	Phe	Val	L.v.s	Met	Glu
65					70			_,_		75			-,-		80
Ser	Val	Glu	Glu	Phe	Glu	G1y	Leu	Asp	Ser	Pro	Glu	Phe	Glu	Asn	Val
				85					90					95	
Phe	Val	Val	Thr	Asp	Phe	Gln	Asp	Ser	Val	Phe	Asn	Asp	Leu	Tyr	Lys
			100					105					110		
Ala	Asp	Cys	Arg	Val	Ile	G1y	Pro	Pro	Val	Val	Leu	Asn	Cys	Ser	G1n
		115					120					125			
Lys	Gly	Glu	Pro	Leu	Pro	Phe	Ser	Cys	Arg	Pro	Leu	Tyr	Cys	Thr	Ser
	130					135					140				
Met	Met	Asn	Leu	Val	Leu	Cys	Phe	Thr	Gly	Phe	Arg	Lys	Lys	Glu	Glu
145					150					155					160
Leu	Val	Arg	Leu	Val	Thr	Leu	Val	His	His	Met	Gly	Gly	Val	Ile	Arg

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165 170 175

Lys Asp Phe Asn Ser Lys Val Thr His Leu Val Ala Asn Cys Thr Gln
180 185 190

Gly Glu Lys Phe Arg Val Ala Val Ser Leu Gly Thr Pro Ile Met Lys 195 200 205

Pro Glu Trp Ile Tyr Lys Ala Trp Glu Arg Arg Asn Glu Gln Asp Phe 210 215 220

Tyr Ala Ala Val Asp Asp Phe Arg Asn Glu Phe Lys Val Pro Pro Phe 225 230 235 240

Gln Asp Cys Ile Phe Ser Phe Leu Gly Phe Ser Asp Glu Glu Lys Thr
245 250 255

Asn Met Glu Glu Met Thr Glu Met Gln Gly Gly Lys Tyr Leu Pro Leu
260 265 270

Gly Asp Glu Arg Cys Thr His Leu Val Val Glu Glu Asn Ile Val Lys 275 280 285

Asp Leu Pro Phe Glu Pro Ser Lys Lys Leu Tyr Val Val Lys Gln Glu 290 295 300

Trp Phe Trp Gly Ser Ile Gln Met Asp Ala Arg Ala Gly Glu Thr Met 305 310 315 320

Tyr Leu Tyr Glu Lys Ala Asn Thr Pro Glu Leu Lys Lys Ser Val Ser

325 330 335

Met Leu Ser Leu Asn Thr Pro Asn Ser Asn Arg Lys Arg Arg Arg Leu 340 345 350

Lys Glu Thr Leu Ala Gln Leu Ser Arg Asp Thr Asp Val Ser Pro Phe 355 360 365

Pro Pro Arg Lys Arg Pro Ser Ala Glu His Ser Leu Ser Ile Gly Ser 370 375 380

Leu Leu Asp Ile Ser Asn Thr Pro Glu Ser Ser Ile Asn Tyr Gly Asp 385 390 395 400

Thr Pro Lys Ser Cys Thr Lys Ser Ser Lys Ser Ser Thr Pro Val Pro
405 410 415

Ser Lys Gln Ser Ala Arg Trp Gln Val Ala Lys Glu Leu Tyr Gln Thr
420 425 430

Glu Ser Asn Tyr Val Asn Ile Leu Ala Thr Ile Ile Gln Leu Phe Gln
435 440 445

Val Pro Leu Glu Glu Glu Gly Gln Arg Gly Gly Pro Ile Leu Ala Pro 450 455 460

Glu Glu Ile Lys Thr Ile Phe Gly Ser Ile Pro Asp Ile Phe Asp Val 465 470 475 480 152/735

His	Thr	Lys	Ile	Lys	Asp	Asp	Leu	G1u	Asp	Leu	Ile	Val	Asn	Trp	Asp
				485					490					495	•

- Glu Ser Lys Ser Ile Gly Asp Ile Phe Leu Lys Tyr Ser Lys Asp Leu
 500 505 510
- Val Lys Thr Tyr Pro Pro Phe Val Asn Phe Phe Glu Met Ser Lys Glu 515 520 525
- Thr Ile Ile Lys Cys Glu Lys Gln Lys Pro Arg Phe His Ala Phe Leu 530 535 540
- Lys Ile Asn Gln Ala Lys Pro Glu Cys Gly Arg Gln Ser Leu Val Glu 545 550 555 560
- Leu Leu Ile Arg Pro Val Gln Arg Leu Pro Ser Val Ala Leu Leu Leu 565 570 575
- Asn Asp Leu Lys Lys His Thr Ala Asp Glu Asn Pro Asp Lys Ser Thr
 580 585 590
- Leu Glu Lys Ala Ile Gly Ser Leu Lys Glu Val Met Thr His Ile Asn 595 600 605
- Glu Asp Lys Arg Lys Thr Glu Ala Gln Lys Gln Ile Phe Asp Val Val 610 615 620
- Tyr Glu Val Asp Gly Cys Pro Ala Asn Leu Leu Ser Ser His Arg Ser 153/735

WO 02/053737			PCT/JP01/11389
625	630	635	640

Leu Val Gln Arg Val Glu Thr Ile Ser Leu Gly Glu His Pro Cys Asp
645 650 655

Arg Gly Glu Gln Val Thr Leu Phe Leu Phe Asn Asp Cys Leu Glu Ile
660 665 670

Ala Arg Lys Arg His Lys Val Ile Gly Thr Phe Arg Ser Pro His Gly
675 680 685

Gln Thr Arg Pro Pro Ala Ser Leu Lys His Ile His Leu Met Pro Leu 690 695 700

Ser Gln Ile Lys Lys Val Leu Asp Ile Arg Glu Thr Glu Asp Cys His
705 710 715 720

Asn Ala Phe Ala Leu Leu Val Arg Pro Pro Thr Glu Gln Ala Asn Val
725 730 735

Leu Leu Ser Phe Gln Met Thr Ser Asp Glu Leu Pro Lys Glu Asn Trp
740 745 750

Leu Lys Met Leu Cys Arg His Val Ala Asn Thr Ile Cys Lys Ala Asp
755 760 765

Ala Glu Asn Leu Ile Tyr Thr Ala Asp Pro Glu Ser Phe Glu Val Asn 770 775 780

Thr Lys Asp Met Asp Ser Thr Leu Ser Arg Ala Ser Arg Ala Ile Lys
785 790 795 800

Lys Thr Ser Lys Lys Val Thr Arg Ala Phe Ser Phe Ser Lys Thr Pro 805 810 815

Lys Arg Ala Leu Arg Arg Ala Leu Met Thr Ser His Gly Ser Val Glu 820 825 830

Gly Arg Ser Pro Ser Ser Asn Asp Lys His Val Met Ser Arg Leu Ser 835 840 845

Ser Thr Ser Ser Leu Ala Gly Ile Pro Ser Pro Ser Leu Val Ser Leu 850 855 860

Pro Ser Phe Phe Glu Arg Arg Ser His Thr Leu Ser Arg Ser Thr Thr 865 870 875 885

His Leu Ile

<210> 52

<211> 3910

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

155/735

<222> (29).. (2677)

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1

5

tcc act act ggg agg act agc ttg gca gac tct tcc att ttt gat tct 100
Ser Thr Thr Gly Arg Thr Ser Leu Ala Asp Ser Ser Ile Phe Asp Ser
10 15 20

aaa gtt act gag att tcc aag gaa aac tta ctt att gga tct act tca 148 Lys Val Thr Glu Ile Ser Lys Glu Asn Leu Leu Ile Gly Ser Thr Ser 25 30 35 40

tat gta gaa gaa gag atg cct cag att gaa aca aga gtg ata ttg gtt 196

Tyr Val Glu Glu Met Pro Gln Ile Glu Thr Arg Val Ile Leu Val

45 50 55

caa gaa gct gga aaa caa gaa gaa ctt aca aaa gcc tta aag gac att 244
Gln Glu Ala Gly Lys Gln Glu Glu Leu Thr Lys Ala Leu Lys Asp Ile
60 65 70

aaa gtg ggc ttt gta aag atg gag tca gtg gaa gaa ttt gaa ggt ttg 292 Lys Val Gly Phe Val Lys Met Glu Ser Val Glu Glu Phe Glu Gly Leu 75 80 85

gat tot ocg gaa tit gaa aat gia tit gia gio acg gao tit oag gat 340 Asp Ser Pro Glu Phe Glu Asn Val Phe Val Val Thr Asp Phe Gln Asp 156/735 90 95 100

tct gtc ttt aat gac ctc tac aag gct gat tgt aga gtt att gga cca 388

Ser Val Phe Asn Asp Leu Tyr Lys Ala Asp Cys Arg Val Ile Gly Pro
105 110 115 120

cca gtt gta tta aat tgt tca caa aaa gga gag cct ttg cca ttt tca 436

cca gtt gta tta aat tgt tca caa aaa gga gag cct ttg cca ttt tca 436
Pro Val Val Leu Asn Cys Ser Gln Lys Gly Glu Pro Leu Pro Phe Ser

125 130 135

tgt cgc ccg ttg tat tgt aca agt atg atg aat cta gta cta tgc ttt 484

Cys Arg Pro Leu Tyr Cys Thr Ser Met Met Asn Leu Val Leu Cys Phe

140 145 150

act gga ttt agg aaa aaa gaa gaa cta gtc agg ttg gtg aca ttg gtc 532

Thr Gly Phe Arg Lys Lys Glu Glu Leu Val Arg Leu Val Thr Leu Val

155 160 165

cat cac atg ggt gga gtt att cga aaa gac ttt aat tca aaa gtt aca 580 His His Met Gly Gly Val Ile Arg Lys Asp Phe Asn Ser Lys Val Thr 170 175 180

cat ttg gtg gca aat tgt aca caa gga gaa aaa ttc agg gtt gct gtg 628 His Leu Val Ala Asn Cys Thr Gln Gly Glu Lys Phe Arg Val Ala Val 185 190 195 200

agt cta ggt act cca att atg aag cca gaa tgg att tat aaa gct tgg 676

Ser Leu Gly Thr Pro Ile Met Lys Pro Glu Trp Ile Tyr Lys Ala Trp

205 210 215

157/735

gaa	agg	cgg	aat	gaa	cag	gat	ttc	tat	gca	gca	gtt	gat	gac	ttt	aga	724
				Glu												
			220			•		225				•	230			
aat	σaa	+++	222	gtt	cct	cca	+++	caa	σat	tat	att	+++	aot	ttc	cto	772
				Val												,,,
ASII	Glu		LyS	Val	110	110		GIII	nsp	Cys	116		Ser	1 116	Leu	
		235					240					245				
																000
				gaa												820
Gly		Ser	Asp	G1u	Glu	Lys	Thr	Asn	Met	Glu	Glu	Met	Thr	Glu	Met	
	250					255					260					
caa	gga	ggt	aaa	tat	tta	ccg	ctt	gga	gat	gaa	aga	tgc	act	cac	ctt	868
Gln	Gly	Gly	Lys	Tyr	Leu	Pro	Leu	G1y	Asp	Glu	Arg	Cys	Thr	His	Leu	
265					270					275					280	
gta	gtt	gaa	gag	aat	ata	gta	aaa	gat	ctt	ссс	ttt	gaa	cct	tca	aag	916
Val	Val	Glu	Glu	Asn	Ile	Val	Lys	Asp	Leu	Pro	Phe	Glu	Pro	Ser	Lys	
				285					290					295		
aaa	ctt	tat	gtt	gtc	aag	caa	gag	tgg	ttc	tgg	gga	agc	att	caa	atg	964
Lys	Leu	Tyr	Val	Val	Lys	Gln	Glu	Trp	Phe	Trp	Gly	Ser	Ile	Gln	Met	
			300					305					310			
gat	gcc	cga	gct	gga	gaa	act	atg	tat	tta	tat	gaa	aag	gca	aat	act	1012
				Gly												
,,op	.114	315	1110	0 ± y	Jiu	1111	320		20u	.,.	Jiu	325				
		919					<i>520</i>					JZÜ				

cct	gag	ctc	aag	aaa	tca	gtg	tca	atg	ctt	tct	cta	aat	acc	cct	aac	1060
ro	G1u	Leu	Lys	Lys	Ser	Val	Ser	Met	Leu	Ser	Leu	Asn	Thr	Pro	Asn	
	330					335					340					
agc	aat	cgc	aaa	cga	cgt	cgt	tta	aaa	gaa	aca	ctt	gct	cag	ctt	tca	1108
Ser	Asn	Arg	Lys	Arg	Arg	Arg	Leu	Lys	Glu	Thr	Leu	Ala	Gln	Leu	Ser	
345					350					355					360	
aga	gat	aca	gac	gtg	tca	cca	ttt	cca	ccc	cgt	aag	cgc	cca	tca	gct	1156
Arg	qaA	Thr	Asp	Val	Ser	Pro	Phe	Pro	Pro	Arg	Lys	Arg	Pro	Ser	Ala	
				365					370					375		
gag	cat	tcc	ctt	tcc	ata	ggg	tca	ctc	cta	gat	atc	tcc	aac	aca	cca	1204
Glu	His	Ser	Leu	Ser	Ile	Gly	Ser	Leu	Leu	Asp	Ile	Ser	Asn	Thr	Pro	
			380					385					390			
gag	tct	agc	att	aac	tat	gga	gac	acc	cca	aag	tct	tgt	act	aag	tct	1252
Glu	Ser	Ser	Ile	Asn	Tyr	G1y	Asp	Thr	Pro	Lys	Ser	Cys	Thr	Lys	Ser	
		395					400					405				
tct	aaa	agc	tcc	act	cca	gtt	cct	tca	aag	cag	tca	gca	agg	tgg	caa	1300
Ser	Lys	Ser	Ser	Thr	Pro	Val	Pro	Ser	Lys	Gln	Ser	Ala	Arg	Trp	G1n	
	410					415					420					
gtt	gca	aaa	gag	ctt	tat	caa	act	gaa	agt	aat	tat	gtt	aat	ata	ttg	1348
Val	Ala	Lys	G1u	Leu	Tyr	Gln	Thr	Glu	Ser	Asn	Tyr	Va1	Asn	Ile	Leu	
125					430					435					440	
gca	aca	att	att	cag	tta	ttt	caa	_		ttg	gaa	gag	gaa	gga	caa	1396
								159	735							

Ala	Thr	Ile	Ile	Gln	Leu	Phe	G1n	Val	Pro	Leu	Glu	Glu	Glu	Gly	G1n	
				445					450	,				455		
cgt	ggt	gga	cct	atc	ctt	gca	cca	gag	gag	att	aag	act	att	ttt	ggt	1444
Arg	Gly	Gly	Pro	Ile	Leu	Ala	Pro	G1u	Glu	Ile	Lys	Thr	Ile	Phe	Gly	
			460					465					470			
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agc	atc	cca	gat	atc	ttt	gat	gta	cac	act	aag	ata	aag	gat	gat	ctt	1492
Ser	Ile	Pro	Asp	Ile	Phe	Asp	Val	His	Thr	Lys	Ile	Lys	Asp	Asp	Leu	
		475					480					485				
gaa	gac	ctt	ata	gtt	aat	tgg	gat	gag	agc	aaa	agc	att	ggt	gac	att	1540
Glu	_	Leu	Ile	Val	Asn	Trp	Asp	Glu	Ser	Lys		Ile	Gly	Asp	Ile	
	490					495					500					
																1 505
					aaa											1588
	Leu	Lys	Tyr	Ser	Lys	Asp	Leu	Val	Lys		Tyr	Pro	Pro	Phe		
505					510					515					520	
																1000
					agc											1636
Asn	Phe	Pne	GIU		Ser	Lys	GIU	ınr		TIE	Lys	Cys	GIU		GIU	
				525					530					535		
000	000	0.00	+++	oot	gct	+++	cto	220	ata	220		aca	ดอล	cca	gaa	1684
		•			Ala									_		1001
Lys	110	мg	540	1113	MIG	1110	Deu	545	110	non	OIII	1114	550	110	oru	
			040					040								
t.et.	gga	cgg	cag	agc	ctt	gtt	gaa	ctt	ctt	atc	cga	cca	gta	cag	agg	1732
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0,0		6	-211				- * *		/735		0				•	

WO 02/053737 PCT/JP01/11389
555 560 565

tta ccc agt gtt gca tta ctt tta aat gat ctt aag aag cat aca gct 1780

Leu Pro Ser Val Ala Leu Leu Leu Asn Asp Leu Lys Lys His Thr Ala

570 575 580

gat gaa aat cca gac aaa agc act tta gaa aaa gct att gga tca ctg 1828 Asp Glu Asn Pro Asp Lys Ser Thr Leu Glu Lys Ala Ile Gly Ser Leu 585 590 595 600

aag gaa gta atg acg cat att aat gag gat aag aga aaa aca gaa gct 1876 Lys Glu Val Met Thr His Ile Asn Glu Asp Lys Arg Lys Thr Glu Ala 605 610 615

caa aag caa att ttt gat gtt gtt tat gaa gta gat gga tgc cca gct 1924 Gln Lys Gln Ile Phe Asp Val Val Tyr Glu Val Asp Gly Cys Pro Ala 620 625 630

aat ctt tta tct tct cac cga agc tta gta cag cgg gtt gaa aca att 1972
Asn Leu Leu Ser Ser His Arg Ser Leu Val Gln Arg Val Glu Thr Ile
635 640 645

tct cta ggt gag cac ccc tgt gac aga gga gaa caa gta act ctc ttc 2020 Ser Leu Gly Glu His Pro Cys Asp Arg Gly Glu Gln Val Thr Leu Phe 650 655 660

ctc ttc aat gat tgc cta gag ata gca aga aaa cgg cac aag gtt att 2068

Leu Phe Asn Asp Cys Leu Glu Ile Ala Arg Lys Arg His Lys Val Ile

665 670 675 680

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ggc	act	ttt	agg	agt	cct	cat	ggc	caa	acc	cga	ccc	cca	gct	tct	ctt	2116
Gly	Thr	Phe	Arg	Ser	Pro	His	Gly	Gln	Thr	Arg	Pro	Pro	Ala	Ser	Leu	
				685					690					695		
aag	cat	att	cac	cta	atg	cct	ctt	tct	cag	att	aag	aag	gta	ttg	gac	2164
Lys	His	Ile	His	Leu	Met	Pro	Leu	Ser	Gln	Ile	Lys	Lys	Val	Leu	Asp	
			700					705					710			
ata	aga	gag	aca	gaa	gat	tgc	cat	aat	gct	ttt	gcc	ttg	ctt	gtg	agg	2212
Ile	Arg	Glu	Thr	Glu	Asp	Cys	His	Asn	Ala	Phe	Ala	Leu	Leu	Val	Arg	
		715					720					725				
cca	cca	aca	gag	cag	gca	aat	gtg	cta	ctc	agt	ttc	cag	atg	aca	tca	2260
Pro	Pro	Thr	Glu	Gln	Ala	Asn	Val	Leu	Leu	Ser	Phe	Gln	Met	Thr	Ser	
	730					735					740					
gat	gaa	ctt	cca	aaa	gaa	aac	tgg	cta	aag	atg	ctg	tgt	cga	cat	gta	2308
Asp	Glu	Leu	Pro	Lys	Glu	Asn	Trp	Leu	Lys	Met	Leu	Cys	Arg	His	Val	
745					750					755					760	
gct	aac	acc	att	tgt	aaa	gca	gat	gct	gag	aat	ctt	att	tat	act	gct	2356
Ala	Asn	Thr	Ile	Cys	Lys	Ala	Asp	Ala	Glu	Asn	Leu	Ile	Tyr	Thr	Ala	
				765					770					775	•	
gat	cca	gaa	tcc	ttt	gaa	gta	aat	aca	aaa	gat	atg	gac	agt	aca	ttg	2404
	Pro											•				
F			780					785	•	•		•	790			

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tttaatagtt aactgactat agattgtttt ctatgccatg tatgtgccac ttctgagagt 3837

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<212> PRT

<213> Homo sapiens

<400> 53

Met Glu Gly Pro Gly Leu Gly Ser Gln Cys Arg Asn His Ser His Gly

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Pro His Pro Pro Gly Phe Gly Arg Tyr Gly Ile Cys Ala His Glu Asn 20 25 30

Lys Glu Leu Ala Asn Ala Arg Glu Ala Leu Pro Leu Ile Glu Asp Ser 35 40 45

Ser Asn Cys Asp Ile Val Lys Ala Thr Gln Tyr Gly Ile Phe Glu Arg 50 55 60

Cys Lys Glu Leu Val Glu Ala Gly Tyr Asp Val Arg Gln Pro Asp Lys
65 70 75 80
165/735

Glu	Asn	Val	Ser	Leu	Leu	His	Trp	Ala	Ala	Ile	Asn	Asn	Arg	Leu	Asp
				85					90					95	•

- Leu Val Lys Phe Tyr Ile Ser Lys Gly Ala Val Val Asp Gln Leu Gly
 100 105 110
- Gly Asp Leu Asn Ser Thr Pro Leu His Trp Ala Ile Arg Gln Gly His
 115 120 125
- Leu Pro Met Val IIe Leu Leu Gln His Gly Ala Asp Pro Thr Leu
 130 135 140
- Ile Asp Gly Glu Gly Phe Ser Ser Ile His Leu Ala Val Leu Phe Gln
 145 150 155 160
- His Met Pro Ile Ile Ala Tyr Leu Ile Ser Lys Gly Gln Ser Val Asn 165 170 175
- Met Thr Asp Val Asn Gly Gln Thr Pro Leu Met Leu Ser Ala His Lys
 180 185 190
- Val Ile Gly Pro Glu Pro Thr Gly Phe Leu Leu Lys Phe Asn Pro Ser 195 200 205
- Leu Asn Val Val Asp Lys Ile His Gln Asn Thr Pro Leu His Trp Ala 210 215 220
- Val Ala Ala Gly Asn Val Asn Ala Val Asp Lys Leu Leu Glu Ala Gly 166/735

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225					230					235					240
Ser	Ser	Leu	Asp	Ile 245	Gln	Asn	Val	Lys	Gly 250	G1u	Thr	Pro	Leu	Asp 255	Met
Ala	Leu	Gln	Asn 260	Lys	Asn	Gln	Leu	Ile 265	Ile	His	Met	Leu	Lys 270	Thr	G1u
Ala	Lys	Met 275	Arg	Ala	Asn	Gln	Lys 280	Phe	Arg	Leu	Trp	Arg 285	Trp	Leu	G1n
Lys	Cys 290	G1u	Leu	Phe	Leu	Leu 295	Leu	Met	Leu	Ser	Val 300	Ile	Thr	Met	Trp
Ala 305	Ile	G1y	Tyr	Ile	Leu 310	Asp	Phe	Asn	Ser	Asp 315	Ser	Trp	Leu	Leu	Lys 320
Gly	Cys	Leu	Leu	Val 325	Thr	Leu	Phe	Phe	Leu 330	Thr	Ser	Leu	Phe	Pro 335	Arg
Phe	Leu	Val	Gly 340	Tyr	Lys	Asn	Leu	Val 345	Tyr	Leu	Pro	Thr	Ala 350	Phe	Leu
Leu	Ser	Ser 355	Val	Phe	Trp	Ile	Phe 360	Met	Thr	Trp	Phe	Ile 365	Leu	Phe	Phe
Pro	Asp	Leu	Ala	Gly	Ala	Pro 375	Phe	Tyr	Phe	Ser	Phe	Ile	Phe	Ser	Ile

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Val Ala Phe Leu Tyr Phe Phe Tyr Lys Thr Trp Ala Thr Asp Pro Gly
385 390 395 400

Phe Thr Lys Ala Ser Glu Glu Glu Lys Lys Val Asn Ile Ile Thr Leu
405 410 415

Ala Glu Thr Gly Ser Leu Asp Phe Arg Thr Phe Cys Thr Ser Cys Leu
420 425 430

Ile Arg Lys Pro Leu Arg Ser Leu His Cys His Val Cys Asn Cys Cys
435
440
445

Val Ala Arg Tyr Asp Gln His Cys Leu Trp Thr Gly Arg Cys Ile Gly
450 455 460

Phe Gly Asn His His Tyr Tyr Ile Phe Phe Leu Phe Phe Leu Ser Met 465 470 475 480

Val Cys Gly Trp Ile Ile Tyr Gly Ser Phe Ile Tyr Leu Ser Ser His
485 490 495

Cys Ala Thr Thr Phe Lys Glu Asp Gly Leu Trp Thr Tyr Leu Asn Gln
500 505 510

Ile Val Ala Cys Ser Pro Trp Val Leu Tyr Ile Leu Met Leu Ala Thr
515 520 525

Phe His Phe Ser Trp Ser Thr Phe Leu Leu Leu Asn Gln Leu Phe Gln
530 535 540
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Ile Ala Phe Leu Gly Leu Thr Ser His Glu Arg Ile Ser Leu Gln Lys
545 550 555 560

Gln Ser Lys His Met Lys Gln Thr Leu Ser Leu Arg Lys Thr Pro Tyr
565 570 575

Asn Leu Gly Phe Met Gln Asn Leu Ala Asp Phe Phe Gln Cys Gly Cys
580 585 590

Phe Gly Leu Val Lys Pro Cys Val Val Asp Trp Thr Ser Gln Tyr Thr
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Met Val Phe His Pro Ala Arg Glu Lys Val Leu Arg Ser Val 610 615 620

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<211> 2426

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<220>

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<400> 54

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_		-		_	·		- •				- 3		Glu				
												1		•			
												-					
00 0	cte	ggc	tcg	cag	tgc	agg	aat	cac	agc	cat	ggc	ccc	cac	cct	cca	163	
			Ser			•											
5		,			10	0				15	,				20		
gga	ttt	ggt	cga	tat	ggc	atc	tgt	gca	cat	gaa	aac	aaa	gaa	ctt	gcc	211	
			Arg														
		•	J	25	•		•		30			•		35			
aat	gca	aga	gaa	gct	ctt	cct	ctt	ata	gag	gac	tct	agt	aac	tgt	gac	259	
			Glu														
			40					45					50				
																	•
att	gtc	aaa	gct	act	caa	tac	gga	att	ttt	gaa	cga	tgt	aaa	gag	ttg	307	
Ile	Val	Lys	Ala	Thr	G1n	Tyr	Gly	Ile	Phe	G1u	Arg	Cys	Lys	Glu	Leu		
		55					60					65					
gta	gaa	gca	gga	tat	gat	gtc	agg	caa	cca	gat	aaa	gaa	aat	gtg	tcg	355	
Val	Glu	Ala	G1y	Tyr	Asp	Val	Arg	G1n	Pro	Asp	Lys	G1u	Asn	Val	Ser		
	70					75					80				•		
ctt	ctt	cat	tgg	gct	gct	att	aac	aac	aga	ctg	gat	ctt	gta	aag	ttt	403	
Leu	Leu	His	Trp	Ala	Ala	Ile	Asn	Asn	Arg	Leu	Asp	Leu	Val	Lys	Phe		
85					90					95					100		
tat	att	tca	aaa	ggt	gct	gtt	gta	gat	cag	ttg	ggt	gga	gat	tta	aat	451	
								170/		_							

Tyr Ile Ser Lys Gly Ala Val Val Asp Gln Leu Gly Gly Asp Leu Asn

				105					110					115		
					tgg Trp											499
			120					125					130			
					cat											547
шe	Leu	135	Leu	GIII	His	GIY	140	ASP	F10	HT.	Leu	145	ASP	GIY	GIU	
gga	ttc	agc	agc	atc	cac	ctg	gca	gta	ttg	ttt	caa	cac	atg	cct	att	595
Gly	Phe 150	Ser	Ser	Ile	His	Leu 155	Ala	Val	Leu	Phe	Gln 160	His	Met	Pro	Ile	
ata	gca	tat	ctc	atc	tca	aag	gga	cag	agt	gtg	aat	atg	aca	gat	gta	643
Ile 165	Ala	Tyr	Leu	Ile	Ser 170	Lys	G1y	Gln	Ser	Val	Asn	Met	Thr	Asp	Val 180	
22+	~~~	029	202	cet	ctc	ata	+ +a	t .a	act	cac	222	ata	9++	ggg	cca	691
				Pro	Leu				Ala					Gly		
				185					190					195		
					ctt Leu											739
			200					205					210			
					aac Asn											787
								171/	735							

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gta aca ctg ttt ttt ctg aca tct ttg ttt cca agg ttc ttg gtt ggg

Val Thr Leu Phe Phe Leu Thr Ser Leu Phe Pro Arg Phe Leu Val Gly

tat	aag	aac	ctt	gta	tac	tta	cca	aca	gcc	ttt	ctg	cta	agt	tct	gtt	1171
Tyr	Lys	Asn	Leu	Val	Tyr	Leu	Pro	Thr	Ala	Phe	Leu	Leu	Ser	Ser	Val	
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Phe	Trp	Ile	Phe	Met	Thr	Trp	Phe	Ile	Leu	Phe	Phe	Pro	Asp	Leu	Ala	
			360					365					370			
gga	gcc	cct	ttc	tat	ttc	agt	ttc	att	ttc	agc	ata	gta	gcc	ttt	cta	1267
Gly	Ala	Pro	Phe	Tyr	Phe	Ser	Phe	Ile	Phe	Ser	Ile	Val	Ala	Phe	Leu	
		375					380					385				
tac	ttt	ttc	tat	aag	act	tgg	gca	act	gat	cca	ggc	ttc	act	aag	gct	1315
														Lys		
-,-	390		-,-	_,_		395					400					
tet	σaa	₀ 22	ฮลล	ឧឧଫ	ลลล	σtσ	aat	atc	atc	acc	ctt	gca	ซลล	act	ggc.	1363
														Thr		1000
405	oru	Ulu	Olu	Lys	410	141	non	116	110	415	Leu	MIG	Jiu	1111	420	
¥05					410					410					420	
										.						1411
														aag		1411
ser	Leu	Asp	Phe		ınr	Pne	Cys	Inr		Cys	Leu	IIe	Arg	Lys	Pro	
				425					430					435		
															tat	1459
Leu	Arg	Ser	Leu	His	Cys	His	Val	Cys	Asn	Cys	Cys	Va1	Ala	Arg	Tyr	
			440					445					450			

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gat	caa	cac	tgc	ctg	tgg	act	gga	cgg	tgc	ata	ggt	ttt	ggc	aac	cat	1507
Asp	Gln	His	Cys	Leu	Trp	Thr	Gly	Arg	Cys	Ile	Gly	Phe	Gly	Asn	His	
		455					460					465				
cac	tat	tac	ata	ttc	ttc	ttg	ttt	ttc	ctt	tcc	atg	gta	tgt	ggc	tgg	1555
His	Tyr	Tyr	Ile	Phe	Phe	Leu	Phe	Phe	Leu	Ser	Met	Val	Cys	Gly	Trp	
	470					475					480					
att	ata	tat	gga	tct	ttc	atc	tat	ttg	tcc	agt	cat	tgt	gcc	aca	aca	1603
Ile	Ile	Tyr	Gly	Ser	Phe	Ile	Tyr	Leu	Ser	Ser	His	Cys	Ala	Thr	Thr .	
485					490					495					500	
																•
ttc	aaa	gaa	gat	gga	tta	tgg	act	tac	ctc	aat	cag	att	gtg	gcc	tgt	1651
Phe	Lys	G1u	Asp		Leu	Trp	Thr	Tyr	Leu	Asn	Gln	Ile	Val	Ala	Cys	
				505					510					515		
														ttc		1699
Ser	Pro	Trp		Leu	Tyr	lle	Leu		Leu	Ala	Thr	Phe		Phe	Ser	
			520					525					530			
+~~	+		+++	++-	++0	++-	00+		a+ a	+++		o++	~~~	+++	o+~	1747
														ttt Phe		1747
пъ	Set	535	Lile	Leu	Leu	Leu	540	GIII	Leu	1 116	0111	545	лıа	1 116	Leu	
		300					040					040				
ggr.	ctø	acc	tec	cat	ឧឧଟ	aga	atc	age	ctø	Cap	ลลต	cag	agc	aag	cat	1795
														Lys		1,00
01)	550	****	501		02-	555	110	DOI	Dou	0111	560	-		_,,		
	230															
atø	aaa	cag	acg	ttg	tcc	ctc	866	ลลฐ	aca	cca	tac	aat	ctt	gga	ttc	1843
		0	20				-36	174/							_	

Met Lys Gln Thr Leu Ser Leu Arg Lys Thr Pro Tyr Asn Leu Gly Phe 565 570 575 580

atg cag aac ctg gca gat ttc ttt cag tgt ggc tgc ttt ggc ttg gtg 1891

Met Gln Asn Leu Ala Asp Phe Phe Gln Cys Gly Cys Phe Gly Leu Val

585 590 595

aag ccc tgt gtg gta gat tgg aca tca cag tac acc atg gtc ttt cac 1939

Lys Pro Cys Val Val Asp Trp Thr Ser Gln Tyr Thr Met Val Phe His

600 605 610

cca gcc agg gag aag gtt ctt cgc tca gta tgaagaaaag caacccaaaa 1989
Pro Ala Arg Glu Lys Val Leu Arg Ser Val
615 620

atttagaatt cacctaagtc caaaggaaaa cacgtggttt ttaaagccat taggtaaaaa 2109
aagttctcaa taaaggcatt acaatttttt aggtttagaa agatggactt ttctgataaa 2169
tcttggcaga catctaaaaa aaaaaccata ttttcacaa gaaaatgcaa gttactttt 2229
ttggaaataa tactcactga ttatggataa aatggaatat tttcagatac tatattggct 2289
gtttcaaaat agtactattc tttaaacttg taatttttgc taagttattt gtctttgttg 2349
tatctataaa tatgtaaaaa atatttaaat agatgtacct gttttgcttt cacacttaat 2409

aaaaaatttt tttttgt 2426

<210> 55

<211> 257

<212> PRT

<213> Homo sapiens

<400> 55

Met Ala Ser Lys Ile Gly Ser Arg Arg Trp Met Leu Gln Leu Ile Met

1 5 10 15

Gln Leu Gly Ser Val Leu Leu Thr Arg Cys Pro Phe Trp Gly Cys Phe
20 25 30

Ser Gln Leu Met Leu Tyr Ala Glu Arg Ala Glu Ala Arg Arg Lys Pro 35 40 45

Asp Ile Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala Val Leu 50 55 60

Cys Ala Ser Phe Met Ser Phe Gly Val Lys Arg Arg Trp Phe Ala Leu 65 70 75 80

Gly Ala Ala Leu Gln Leu Ala Ile Ser Thr Tyr Ala Ala Tyr Ile Gly 85 90 95

Gly Tyr Val His Tyr Gly Asp Trp Leu Lys Val Arg Met Tyr Ser Arg

100
105
110
176/735

Thr	Val	Ala	Ile	Ile	G1y	Gly	Phe	Leu	Val	Leu	Ala	Ser	Gly	Ala	Gly
		115					120					125			

- Glu Leu Tyr Arg Arg Lys Pro Arg Ser Arg Ser Leu Gln Ser Thr Gly
 130 135 140
- His Ser Lys Glu Asp Arg Leu Ala Tyr Leu Asn His Leu Pro Gly Gly
 165 170 175
- Glu Leu Met Ile Gln Leu Phe Phe Val Leu Tyr Gly Ile Leu Ala Leu 180 185 190
- Ala Phe Leu Ser Gly Tyr Tyr Val Thr Leu Ala Ala Gln Ile Leu Ala 195 200 205
- Val Leu Leu Pro Pro Val Met Leu Leu Ile Asp Gly Asn Val Ala Tyr 210 215 220
- Trp His Asn Thr Arg Arg Val Glu Phe Trp Asn Gln Met Lys Leu Leu 225 230 235 240
- Gly Glu Ser Val Gly Ile Phe Gly Thr Ala Val Ile Leu Ala Thr Asp 245 250 255

Gly

<210> 56

<211> 1520

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (10).. (780)

<400> 56

tttcccaag atg gcg tcg aag ata ggt tcg aga cgg tgg atg ttg cag ctg 51 Met Ala Ser Lys Ile Gly Ser Arg Arg Trp Met Leu Gln Leu

1 5 10

atc atg cag ttg ggt tcg gtg ctg ctc aca cgc tgc ccc ttt tgg ggc 99

Ile Met Gln Leu Gly Ser Val Leu Leu Thr Arg Cys Pro Phe Trp Gly

15 20 25 30

tgc ttc agc cag ctc atg ctg tac gct gag agg gct gag gca cgc cgg 147

Cys Phe Ser Gln Leu Met Leu Tyr Ala Glu Arg Ala Glu Ala Arg Arg

35 40 45

aag ccc gac atc cca gtg cct tac ctg tat ttc gac atg ggg gca gcc 195

Lys Pro Asp Ile Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala

50 55 60

178/735

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gtg	ctg	tgc	gct	agt	ttc	atg	tcc	ttt	ggc	gtg	aag	cgg	cgc	tgg	ttc	243
Val	Leu	Cys	Ala	Ser	Phe	Met	Ser	Phe	Gly	Val	Lys	Arg	Arg	Trp	Phe	
		65					70					75				
gcg	ctg	ggg	gcc	gca	ctc	caa	ttg	gcc	att	agc	acc	tac	gcc	gcc	tac	291
Ala	Leu	Gly	Ala	Ala	Leu	G1n	Leu	Ala	Ile	Ser	Thr	Tyr	Ala	Ala	Tyr	
	80					85					90				•	
atc	ggg	ggc	tac	gtc	cac	tac	ggg	gac	tgg	ctg	aag	gtc	cgt	atg	tac	339
Ile	Gly	G1y	Tyr	Val	His	Tyr	Gly	Asp	Trp	Leu	Lys	Val	Arg	Met	Tyr	
95					100					105					110	
tcg	cgc	aca	gtt	gcc	atc	atc	ggc	ggc	ttt	ctt	gtg	ttg	gcc	agc	ggt	387
Ser	Arg	Thr	Val	Ala	Ile	Ile	G1y	Gly	Phe	Leu	Val	Leu	Ala	Ser	Gly	
				115					120					125		
		gag														435
Ala	Gly	Glu		Tyr	Arg	Arg	Lys		Arg	Ser	Arg	Ser		Gln	Ser	
			130					135					140		-	
			.		- 4		_4_	.	_ 4		.				.2.	400
		cag														483
ınr	GIY	Gln	vai	Pne	Leu	GIÀ		lyr	Leu	TTE	Cys		Ата	ıyr	Ser	
		145					150					155		•		
cta	090	cac	200	920	222	gan	eaa	cta	aca	†9 †	cta	222	ca+	o+ o	000	531
		His	_													991
ren	160	1112	Det	LJS	OIU	165	мg	Leu	.11G	1 y 1	170	nən	1112	Leu	110	
	100					100					1.0					
gga	ggg	gag	ctø	atø	atc	Cag	ctø	tte	ttc	gtg	cte	tat	ggc	atc	cta	579
95u	555	5ug	- v5	<u> ۵</u> ۷		Jug	- v5	179/		0.0	5	Jul	850	400	~ ∪g	010

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W	WO 02/053737 PCT/JP0														201/11389	
Gly 175	Gly	Glu	Leu	Met	Ile 180	Gln	Leu	Phe	Phe	Val	Leu	Tyr	Gly	Ile	Leu 190	
113					100					100					190	
gcc	ctg	gcc	ttt	ctg	tca	ggc	tac	tac	gtg	acc	ctc	gct	gcc	cag	atc	627
Ala	Leu	Ala	Phe	Leu	Ser	G1y	Tyr	Tyr	Val	Thr	Leu	Ala	Ala	Gln	Ile	
				195					200					205		
ctg	gct	gta	ctg	ctg	ccc	cct	gtc	atg	ctg	ctc	att	gat	ggc	aat	gtt	675
Leu	Ala	Val	Leu	Leu	Pro	Pro	Val	Met	Leu	Leu	Ile	Asp	Gly	Asn	Val	
			210					215					220			
gct	tac	tgg	cac	aac	acg	cgg	cgt	gtt	gag	ttc	tgg	aac	cag	atg	aag	723
Ala	Tyr	Trp	His	Asn	Thr	Arg	Arg	Val	G1u	Phe	Trp	Asn	G1n	Met	Lys	
		225					230					235				
ctc	ctt	gga	gag	agt	gtg	ggc	atc	ttc	gga	act	gct	gtc	atc	ctg	gcc	771
Leu	Leu	Gly	G1u	Ser	Val	Gly	Ile	Phe	Gly	Thr	Ala	Val	Ile	Leu	Ala	
	240			٠		245					250					
act	gat	ggc	tgag	gtttt	at g	gcaa	agagg	gc tg	gagat	gggc	aca	ıggga	agcc			820
Thr	Asp	Gly														
255																
acte	gaggg	gtc a	iccct	gcct	t co	tcct	tgct	ggo	ccag	ctg	ctgt	ttat	tt a	tgct	ttttg	880

tttgtccaaa tttctgggct cagcgcttgg gagggcagga gccctggcac taatgctgta 1000

gtctgtttgt ttgatctttt gctttttaa aattgttttt tgcagttaag aggcagctca 940

caggittitt teetgitagg agagetgagg eeagetgeee aetgagtete etgieeetga 1060
gaagggagta tggeagget gggatgege taetgagat gggagagtgg gagacagagg 1120
aaggaagatg gagattggaa gtgageaaat gtgaaaaatt eetetttgaa eetggeagat 1180
geagetagge tetgeagtge tgittggaga etgtgagagg gagtgtgt gitgacacat 1240
gtggateagg eeeaggaagg geacaggge tgageactae agaagteaca tgggitetea 1300
gggatatgeea ggggeagaaa eagtacegge teetetgieae teaeettgag agtaggagga 1360
accetgitet getetgget gigaagggi ggageaggea giggeeaget tigeeettee 1420
tgetgitetet gittetaget eeatggitgg eetggiggg giggagitee eteecaaaca 1480
ceagaceaca eagteeteea aaaataaaca tittaatag 1520

<210> 57

<211> 107

<212> PRT

<213> Homo sapiens

<400> 57

Met Ala Leu Phe Ala Gly Gly Lys Leu Arg Val His Leu Asp Ile Gln

1 5 10 15

Val Gly Glu His Ala Asn Asn Tyr Pro Glu Ile Ala Ala Lys Asp Lys 181/735

20 25 30

Leu Thr Glu Leu Gln Leu Arg Ala Arg Gln Leu Leu Asp Gln Val Glu
35 40 45

Gln Ile Gln Lys Glu Gln Asp Tyr Gln Arg Tyr Arg Glu Glu Arg Phe
50 55 60

Arg Leu Thr Ser Glu Ser Thr Asn Gln Arg Val Leu Trp Trp Ser Ile
65 70 75 80

Ala Gln Thr Val Ile Leu Ile Leu Thr Gly Ile Trp Gln Met Arg His

85 90 95

Leu Lys Ser Phe Phe Glu Ala Lys Lys Leu Val

<210> 58

<211> 1496

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (9).. (329)

<400> 58

ctaccagg atg gct ctc ttc gct ggt ggc aaa ctg cgt gtg cat ctc gac 50 182/735

Met	Ala	Leu	Phe	Ala	Gly	Gly	Lys	Leu	Arg	Val	His	Leu	Asp
1				5					10				

atc	cag	gtt	ggg	gag	cat	gcc	aac	aac	tac	cct	gag	att	gct	gca	aaa	98
Ile	Gln	Val	Gly	Glu	His	Ala	Asn	Asn	Tyr	Pro	Glu	Ile	Ala	Ala	Lys	
15					20					25					30	
gat	aag	ctg	acg	gag	cta	cag	ctc	cgc	gcc	cgc	cag	ttg	ctt	gat	cag	146

gat aag ctg acg gag cta cag ctc cgc gcc cgc cag ttg ctt gat cag 146
Asp Lys Leu Thr Glu Leu Gln Leu Arg Ala Arg Gln Leu Leu Asp Gln
35 40 45

gtg gaa cag att cag aag gag cag gat tac caa agg tat cgt gaa gag 194
Val Glu Gln Ile Gln Lys Glu Gln Asp Tyr Gln Arg Tyr Arg Glu Glu
50 55 60 .

cgc ttc cga ctg acg agc gag agc acc aac cag agg gtc cta tgg tgg 242

Arg Phe Arg Leu Thr Ser Glu Ser Thr Asn Gln Arg Val Leu Trp Trp

65 70 75

tcc att gct cag act gtc atc ctc atc ctc act ggc atc tgg cag atg 290

Ser Ile Ala Gln Thr Val Ile Leu Ile Leu Thr Gly Ile Trp Gln Met

80 85 90

cgt cac ctc aag agc ttc ttt gag gcc aag aag ctg gtg tagtgccctc 339

Arg His Leu Lys Ser Phe Phe Glu Ala Lys Lys Leu Val

95 100 105

tttgtatgac cetteetttt taceteattt atttggtact tteeceacae agteetttat 399

ccacctggat ttttagggaa aaaaaatgaa aaagaataag tcacattggt tccatggcca 459 caaaccattc agatcagcca cttgctgacc ctggttctta aggacacatg acattagtcc 519 aatctttcaa aatcttgtct tagggcttgt gaggaatcag aactaaccca ggactcagtc 579 ctgcttcttt tgcctcgagt gattttcctc tgtttttcac taaataagca aatgaaaact 639 ctctccatta ccttctgctt tctctttgtc cacttacgca gtaggtgact ggcatgtgcc 699 acagagcagg ccctgcctca ctgtctgctg gtcagttctg ggttcactta atggctttgt 759 gaatgtaaat aaggggcagg tettggeeet agaggattga gatgttttte tatatettag 819 aactattttt ggataaatta tatattttcc ttcctagtag aagtgttact gcctgtaact 879 ageteaaaat accaatgeag tttetgeatt etgggttttg tttttetttt ttttttttt 939 ttttttgagt tttgctcttg tcgcccaggc tggagtgcaa tggcgtgatc tcagctcact 999 ggcaacatct gcctccggg ttcaaatgat tctcctgcct cagtctcctg agtagctggg 1059 attacaggtg cccgccacca cgctcagcta atttttgtat ttttagtaga gatggggttt 1119 taccatgttg gccaggctgg tcttagactc ctgacctcag ttgatccacc tgcctcagcc 1179 tetgeattea gtttatteae atatttttgg taacteecat ggeageteet aggattteag 1239 cggtctgtgg gccagaaagc aggcaccagg gctgacctca aggccgtatc agagggccaa 1299 184/735

gcagagttct tttggatacc tgcttttcat cccacagggc cttagagtca gaggtaaggt 1359
agcaacagag ctagaatggg gcaatgcact cttaccctcc ttctcaactt ttatttaagc 1419
tgtgctaaat gtttcttca agggaaccag atttagttct ttacagaatt ttccagtgaa 1479
ataaaacatg ttgtaat 1496

<210> 59

<211> 272

<212> PRT

<213> Homo sapiens

<400> 59

Met Met Ile His Gly Phe Gln Ser Ser His Arg Asp Phe Cys Phe Gly

1 5 10 15

Pro Trp Lys Leu Thr Ala Ser Lys Thr His Ile Met Lys Ser Ala Asp
20 25 30

Val Glu Lys Leu Ala Asp Glu Leu His Met Pro Ser Leu Pro Glu Met
35 40 45

Met Phe Gly Asp Asn Val Leu Arg Ile Gln His Gly Ser Gly Phe Gly 50 55 60

Ile Glu Phe Asn Ala Thr Asp Ala Leu Arg Cys Val Asn Asn Tyr Gln 185/735

65					70					75					80
Gly	Met	Leu	Lys	Val 85	Ala	Cys	Ala	Glu	Glu 90	Trp	Gln	Glu	Ser	Arg 95	Thr
Glu	Gly	G1u	His 100	Ser	Lys	Glu	Val	Ile 105	Lys	Pro	Tyr	Asp	Trp 110	Thr	Tyr
Thr	Thr	Asp 115	Tyr	Lys	Gly	Thr	Leu 120	Leu	Gly	Glu	Ser	Leu 125	Lys	Leu	Lys
Val	Val 130	Pro	Thr	Thr	Asp	His 135	Ile	Asp	Thr	Glu	Lys 140	Leu	Lys	Ala	Arg
Glu 145	G1n	Ile	Lys	Phe	Phe 150	G1u	Glu	Val	Leu	Leu 155	Phe	Glu	Asp	Glu	Leu 160
His	Asp	His	Gly	Val 165	Ser	Ser	Leu	Ser	Val 170	Lys	Ile	Arg	Val	Met 175	Pro
Ser	Ser	Phe	Phe 180	Leu	Leu	Leu	Arg	Phe 185	Phe	Leu	Arg	Ile	Asp 190	Gly	Val
Leu	Ile	Arg 195	Met	Asn	Asp	Thr	Arg 200	Leu	Tyr	His	Glu	Ala 205	Asp	Lys	Thr
Tyr	Met 210	Leu	Arg	G1u	Tyr	Thr 215	Ser	Arg	Glu	Ser	Lys 220	Ile	Ser	Ser	Leu

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Met His Val Pro Pro Ser Leu Phe Thr Glu Pro Asn Glu Ile Ser Gln 225 230 235 240

Tyr Leu Pro Ile Lys Glu Ala Val Cys Glu Lys Leu Ile Phe Pro Glu 245 250 255

Arg Ile Asp Pro Asn Pro Ala Asp Ser Gln Lys Ser Thr Gln Val Glu 260 265 270

<210> 60

<211> 1916 ·

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (117).. (932)

<400> 60

atggtaacgg ctcggaagcc taggaggctg ggccggaggg aggcggagga accggtgttc 60

geogeogeog etgetteage ttatteettg tggeetetge gggteetgee teagee atg 119

Met 1

·

atg atc cac ggc ttc cag agc agc cac cgg gat ttc tgc ttc ggg ccc 167 Met Ile His Gly Phe Gln Ser Ser His Arg Asp Phe Cys Phe Gly Pro

> 5 10 15 187/735

tgg	aag	ctg	acg	gcg	tcc	aag	acc	cac	atc	atg	aag	tcg	gcg	gat	gtg	215
Trp	Lys	Leu	Thr	Ala	Ser	Lys	Thr	His	Ile	Met	Lys	Ser	Ala	Asp	Val	
		20					25					30				
gag	aaa	tta	gcc	gat	gaa	tta	cat	atg	cca	tct	ctc	cct	gaa	atg	atg	263
Glu	Lys	Leu	Ala	Asp	Glu	Leu	His	Met	Pro	Ser	Leu	Pro	Glu	Met	Met	
	35					40					45					
ttt	gga	gac	aac	gtt	tta	aga	atc	cag	cat	ggg	tct	ggc	ttt	gga	att	311
Phe	Gly	Asp	Asn	Val	Leu	Arg	Ile	Gln	His	Gly	Ser	Gly	Phe	Gly	Ile	
50					55					60					65	
gag	ttc	aat	gct	aca	gat	gcg	tta	aga	tgt	gta	aac	aac	tac	caa	gga	359
Glu	Phe	Asn	Ala	Thr	Asp	Ala	Leu	Arg	Cys	Val	Asn	Asn	Tyr	Gln	Gly	
				70					75					80		
atg	ctt	aaa	gtg	gcc	tgt	gct	gaa	gag	tgg	caa	gaa	agc	agg	acg	gag	407
Met	Leu	Lys	Val	Ala	Cys	Ala	Glu	Glu	Trp	Gln	Glu	Ser	Arg	Thr	Glu	
			85					90					95			
ggt	gaa	cac	tcc	aaa	gag	gtt	att	aaa	cca	tat	gat	tgg	acc	tat	aca	455
Gly	Glu	His	Ser	Lys	Glu	Val	Ile	Lys	Pro	Tyr	Asp	Trp	Thr	Tyr	Thr	
		100					105					110				
aca	gat	tat	aag	gga	acc	tta	ctt	gga	gaa	tct	ctt	aag	tta	aag	gtt	503
Thr	Asp	Tyr	Lys	G1y	Thr	Leu	Leu	G1y	Glu	Ser	Leu	Lys	Leu	Lys	Val	
	115					120					125					

188/735

gta	cct	aca	aca	gat	cat	ata	gat	aca	gaa	aaa	ttg	aaa	gcc	aga	gaa	551
Val	Pro	Thr	Thr	Asp	His	Ile	Asp	Thr	Glu	Lys	Leu	Lys	Ala	Arg	Glu	
130					135					140					145	
cag	att	aag	ttt	ttt	gaa	gaa	gtt	ctc	ctt	ttt	gag	gat	gaa	ctt	cat	599
G1n	Ile	Lys	Phe	Phe	Glu	Glu	Val	Leu	Leu	Phe	Glu	Asp	Glu	Leu	His	
				150					155					160		
gat	cat	gga	gtt	tca	agc	ctg	agt	gtg	aag	att	aga	gta	atg	cct	tct	647
Asp	His	Gly	Val	Ser	Ser	Leu	Ser	Val	Lys	Ile	Arg	Val	Met	Pro	Ser	
			165					170					175			
						cgg										695
Ser	Phe		Leu	Leu	Leu	Arg		Phe	Leu	Arg	Ile		Gly	Val	Leu	
		180					185					190				
						aga										743
Ile		Met	Asn	Asp	Thr	Arg	Leu	Tyr	His	Glu		Asp	Lys	Thr	Tyr	
	195					200					205					
						tca						_	_			791
	Leu	Arg	Glu	Tyr		Ser	Arg	Glu	Ser		He	Ser	Ser	Leu		
210					215					220					225	
				,		44-				,			.			000
						ttc										839
пıs	vaı	Pro	Pro		Leu	Phe	ınr	GIU		Asn	GIU	116	ser		ıyr	
				230					235					240		
.		_4_			455	~++	+ +			_4_	-+-	+++	000	ac-		007
ita	cca	ata	aag	gaa	gca	gtt	Lgt	gag 189/	_	cta	ata		cca	gaa	aga	887

Leu Pro Ile Lys Glu Ala Val Cys Glu Lys Leu Ile Phe Pro Glu Arg
245 250 255

att gat cct aac cca gca gac tca caa aaa agt aca caa gtg gaa 932

Ile Asp Pro Asn Pro Ala Asp Ser Gln Lys Ser Thr Gln Val Glu
260 265 270

taaaatgtga tacaacatat actcactatg gaatctgact ggacaccttg gctatttgta 992 aggggttatt tttattatga gaattaattg ccttgtttat gtacagattt tctgtagcct 1052 taaaggaaaa aaaaataaag atcgttacag gcaggtttca ctcaactgct atttgtactg 1112 tetgtettea catteatatt ceagatttat attttetgga gttaaatttg gatgatttet 1172 aaattatcac aaagtgggac ctcagcagta gtgatgtgtg tgtctcatga gcagtgagca 1232 cagtctgcat tcatcatgaa acactatctt ctaccaggag gaggttaatg taaatcacca 1292 aatcccaatg cettgtgact tteataggat teetgateat geatgttgat gtaetggete 1352 ttcactttgg gctttctgat gtttattcac acctttggag agttgcaact tgccacatac 1412 gaaattagtc tcatagtgta gtgaacttca accccaaaat tttaaaaaatg tatttccccc 1472 cagttttaaa ttgcctttga aatttaaaaa aaaaaattta gacttagtac cagaaccaaa 1532 aatacctaga tttttggaga acttattaca tacatagaaa catgaatatg gtttaccwct 1592

tettggtee tgaatagtee tagattactt attttgagaa ttgattgtta aaaattacag 1712
ggaattaaaa taattgeett ttttttta gagggtaaga gatgggtaga agagtatgee 1772
tetgaaaatt ttattagttt attettgtg agaataccaa gaaaatgtgt atttgeeat 1832
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agaataaaca ataaggaatt actg 1916

<210> 61

<211> 219

<212> PRT

<213> Homo sapiens

<400> 61

Met Asn Arg Leu Phe Gly Lys Ala Lys Pro Lys Ala Pro Pro Pro Ser

1 5 10 15

Leu Thr Asp Cys Ile Gly Thr Val Asp Ser Arg Ala Glu Ser Ile Asp
20 25 30

Lys Lys Ile Ser Arg Leu Asp Ala Glu Leu Val Lys Tyr Lys Asp Gln
35 40 45

Ile Lys Lys Met Arg Glu Gly Pro Ala Lys Asn Met Val Lys Gln Lys 191/735

	50					55					60				
Ala 65	Leu	Arg	Val	Leu	Lys 70	Gln	Lys	Arg	Met		, Glu	Gln	Gln	Arg	Asp 80
Asn	Leu	Ala	G1n	Gln 85	Ser	Phe	Asn	Met	G1u 90	Gln	Ala	Asn	Tyr	Thr 95	Ile
Gln	Ser	Leu	Lys 100	Asp	Thr	Lys	Thr	Thr 105	Val	Asp	Ala	Met	Lys 110	Leu	Gly
Val	Lys	Glu 115	Met	Lys	Lys	Ala	Tyr 120	Lys	G1n	Val	Lys	Ile 125	Asp	Gln	Ile
G1u	Asp 130	Leu	Gln	Asp	G1n	Leu 135	Glu	Asp	Met	Met	Glu 140	Asp	Ala	Asn	Glu
Ile 145	Gln	Glu	Ala	Leu	Ser 150	Arg	Ser	Tyr	G1y	Thr 155	Pro	Glu	Leu	Asp	G1u 160
Asp	Asp	Leu	G1u	Ala 165	Glu	Leu	Asp	Ala	Leu 170	Gly	Asp	Glu	Leu	Leu 175	Ala
Asp	Glu	Asp	Ser 180	Ser	Tyr	Leu	Asp	G1u 185	Ala	Ala	Ser	Ala	Pro 190	Ala	Ile
Pro	Glu	Gly 195	Val	Pro	Thr	Asp	Thr 200	Lys	Asn	Lys	Asp	Gly 205	Val	Leu	Val

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Asp Glu Phe Gly Leu Pro Gln Ile Pro Ala Ser 210 215

<210> 62

<211> 1362

<212> DNA

<213> Homo sapiens

<220>

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<222> (49).. (705)

<400> 62

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Leu Phe Gly Lys Ala Lys Pro Lys Ala Pro Pro Pro Ser Leu Thr Asp

5 10 15

tgc att ggc acg gtg gac agt aga gca gaa tcc att gac aag aag att 153

Cys Ile Gly Thr Val Asp Ser Arg Ala Glu Ser Ile Asp Lys Lys Ile

20 25 30 35

tct cga ttg gat gct gag cta gtg aag tat aag gat cag atc aag aag 201 Ser Arg Leu Asp Ala Glu Leu Val Lys Tyr Lys Asp Gln Ile Lys Lys

> 40 45 50 193/735

atg	aga	gag	ggt	cct	gca	aag	aat	atg	gtc	aag	cag	aaa	gcc	ttg	cga	249
Met	Arg	G1u	G1y	Pro	Ala	Lys	Asn	Met	Val	Lys	Gln	Lys	Ala	Leu	Arg	
			55		•			60					65			
gtt	tta	aag	caa	aag	agg	atg	tat	gag	cag	cag	cgg	gac	aat	ctt	gcc	297
Val	Leu	Lys	G1n	Lys	Arg	Met	Tyr	Glu	Gln	G1n	Arg	Asp	Asn	Leu	Ala	
		70					75					80				
caa	cag	tca	ttc	aac	atg	gaa	caa	gcc	aat	tat	acc	atc	cag	tct	ttg	345
Gln	Gln	Ser	Phe	Asn	Met	Glu	Gln	Ala	Asn	Tyr	Thr	Ile	G1n	Ser	Leu	
	85					90					95					
aag	gac	acc	aag	acc	acg	gtt	gat	gct	atg	aaa	ctg	gga	gta	aag	gaa	393
Lys	Asp	Thr	Lys	Thr	Thr	Val	Asp	Ala	Met	Lys	Leu	Gly	Val	Lys	Glu	
100					105					110					115	
atg	aag	aag	gca	tac	aag	caa	gtg	aag	atc	gac	cag	att	gag	gat	tta	441
Met	Lys	Lys	Ala	Tyr	Lys	G1n	Val	Lys	Ile	Asp	G1n	Ile	Glu	Asp	Leu	
				120					125					130		
caa	gac	cag	cta	gag	gat	atg	atg	gaa	gat	gca	aat	gaa	atc	caa	gaa	489
Gln	Asp	Gln	Leu	G1u	Asp	Met	Met	G1u	Asp	Ala	Asn	Glu	Ile	Gln	Glu	
			135					140					145			
gca	ctg	agt	cgc	agt	tat	ggc	acc	cca	gaa	ctg	gat	gaa	gat	gat	tta	537
Ala	Leu		Arg	Ser	Tyr	Gly	Thr	Pro	Glu	Leu	Asp		Asp	Asp	Leu	
		150					155					160				

gaa gca gag ttg gat gca cta ggt gat gag ctt ctg gct gat gaa gac 585 Glu Ala Glu Leu Asp Ala Leu Gly Asp Glu Leu Leu Ala Asp Glu Asp 165 170 175

agt tot tat ttg gat gag goa goa tot goa cot goa att coa gaa ggt 633

Ser Ser Tyr Leu Asp Glu Ala Ala Ser Ala Pro Ala Ile Pro Glu Gly

180 185 190 195

gtt ccc act gat aca aaa aac aag gat gga gtt ctg gtg gat gaa ttt 681 Val Pro Thr Asp Thr Lys Asn Lys Asp Gly Val Leu Val Asp Glu Phe 200 205 210

gga ttg cca cag atc cct gct tca tagatttgca tcattcaagc atatcttgta 735 Gly Leu Pro Gln Ile Pro Ala Ser

215

aaacaaacac atattatggg actaggaaat atttatcttt ccaaatttgc cataacagat 795

ttaggtttct ttcctttctt tgaaggaaag tttaattaca ttgctctttt atttttcca 855

ttaaggact cattgcttgg gaaatgcttt cttcgtacta aaatttgatt cctttttttt 915

cttatgaaaa acgaactcag tttaaaagta tttttagctc gtatgacttg ttttcattca 975

ttaataataa tttgaaataa aactaaggaa atggaatctt aaaagtctat gacagtgtaa 1035

ctctacagtc tcaaaatgac ctgataaatt gataagacaa agatgagatt attggggctg 1095

ttcatattat gattcagaat cattttctat tgtggtatta taggttggtt aaagtgatgg 1155

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tggaattatc actactgtat catgagtggg tattttgatt ctatggttcc ctcagtatta 1275
catcttgact tgtaatcaat tatgaatatt tcttgatatt taatgtatag gacatttatt 1335
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<210> 63

<211> 622

<212> PRT

<213> Homo sapiens

<400> 63

Met Ala Asp Gly Pro Asp Glu Tyr Asp Thr Glu Ala Gly Cys Val Pro

1 5 10 15

Leu Leu His Pro Glu Glu Ile Lys Pro Gln Ser His Tyr Asn His Gly
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Tyr Gly Glu Pro Leu Gly Arg Lys Thr His Ile Asp Asp Tyr Ser Thr

35 40 45

Trp Asp Ile Val Lys Ala Thr Gln Tyr Gly Ile Tyr Glu Arg Cys Arg
50 55 60

Glu Leu Val Glu Ala Gly Tyr Asp Val Arg Gln Pro Asp Lys Glu Asn 196/735

,	WO 0	2/053	737												PCT/JP01/11389
65					70					75					80
Val	Thr	Leu	Leu	His 85	Trp	Ala	Ala	Ile	Asn 90	Asn	Arg	Ile	Asp	Leu 95	Val
Lys	Tyr	Tyr	Ile 100	Ser	Lys	Gly	Ala	Ile 105	Val	Asp	Gln	Leu	Gly 110	Gly	Asp
Leu	Asn	Ser 115	Thr	Pro	Leu	His	Trp 120	Ala	Thr	Arg	Gln	Gly 125	His	Leu	Ser
Met	Val 130	Val	Gln	Leu	Met	Lys 135	Tyr	Gly	Ala	Asp	Pro 140	Ser	Leu	Ile	Asp
Gly 145	Glu	Gly	Cys	Ser	Cys 150	Ile	His	Leu	Ala	Ala 155	Gln	Phe	Gly	His	Thr 160
Ser	Ile	Val	Ala	Tyr 165	Leu	Ile	Ala	Lys	Gly 170	Gln	Asp	Val	Asp	Met 175	Met
Asp	Gln	Asn	Gly 180	Met	Thr	Pro	Leu	Met 185	Trp	Ala	Ala	Tyr	Arg 190	Thr [°]	His
Ser	Val	Asp 195	Pro	Thr	Arg	Leu	Leu 200	Leu	Thr	Phe	Asn	Val 205	Ser	Val	Asn
Leu	Gly 210	Asp	Lys	Tyr	His	Lys 215	Asn	Thr	Ala	Leu _.	His 220	Trp	Ala	Val	Leu

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VO 02/053737	PCT/JP01/11389
VO 02/053737	

Ala 225	Gly	Asn	Thr	Thr	Val 230	Ile	Ser	Leu	Leu	Leu 235	Glu	Ala	G1y	Ala	Asn 240
Val	Asp	Ala	Gln	Asn 245	Ile	Lys	G1y	Glu	Ser 250	Ala	Leu	Asp	Leu	Ala 255	Lys
G1n	Arg	Lys	Asn 260	Val	Trp	Met	Ile	Asn 265	His	Leu	G1n	Glu	Ala 270	Arg	Gln
Ala	Lys	Gly 275	Tyr	Asp	Asn	Pro	Ser 280	Phe	Leu	Arg	Lys	Leu 285	Lys	Ala	Asp
Lys	Glu 290	Phe	Arg	Gln	Lys	Val 295	Met	Leu	Gly	Thr	Pro 300	Phe	Leu	Val	Ile
Trp 305	Leu	Val	Gly	Phe	Ile 310	Ala	Asp	Leu	Asn	Ile 315	Asp	Ser	Trp	Leu	Ile 320
Lys	Gly	Leu	Met	Tyr 325	Gly	Gly	Val	Trp	Ala 330	Thr	Val	Gln	Phe	Leu 335	Ser
Lys	Ser	Phe	Phe 340	Asp	His	Ser	Met	His 345	Ser	Ala	Leu	Pro	Leu 350	Gly	Ile
Tyr	Leu	Ala 355	Thr	Lys	Phe	Trp	Met 360	Tyr	Val	Thr	Trp	Phe 365	Phe	Trp	Phe

Trp Asn Asp Leu Asn Phe Leu Phe Ile His Leu Pro Phe Leu Ala Asn

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380

375

370

Ser 385	Val	Ala	Leu	Phe	Tyr 390	Asn	Phe	Gly	Lys	Ser 395	Trp	Lys	Ser	Asp	Pro
															200
Gly	Ile	Ile	Lys	Ala	Thr	Glu	Glu	Gln	Lys	Lys	Lys	Thr	Ile	Val	Glu
				405					410					415	
Leu	Ala	Glu	Thr	Gly	Ser	Leu	Asp	Leu	Ser	Ile	Phe	Cys	Ser	Thr	Cys
			420					425					430		
Leu	Ile	Arg	Lys	Pro	Val	Arg	Ser	Lys	His	Cys	Gly	Val	Cys	Asn	Arg
		435					440					445			
Cys	Ile	Ala	Lys	Phe	Asp	His	His	Cys	Pro	Trp	Va1	Gly	Asn	Cys	Val
	450					455					460				
Gly	Ala	G1y	Asn	His	Arg	Tyr	Phe	Met	Gly	Tyr	Leu	Phe	Phe	Leu	Leu
465					470					475					480
Phe	Met	Ile	Cys	Trp	Met	Ile	Tyr	Gly	Cys	Ile	Ser	Tyr	Trp	Gly	Leu
				485					490					495	
Hic	Cvs	G1u	Thr	Thr	Tur	Thr	Ive	Asn	G1 v	Phe	Trn	Thr	Tur	Tla	Thr
1113	0,3	Old	500	1111	1 7 1	1111	Буз	505	OLY	1116	пр	1111	510	116	1111
G1n	Ile	Ala	Thr	Cys	Ser	Pro	Trp	Met	Phe	Trp	Met	Phe	Leu	Asn	Ser
		515					520					525			

Val Phe His Phe Met Trp Val Ala Val Leu Leu Met Cys Gln Met Tyr

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530 535 540

Gln Ile Ser Cys Leu Gly Ile Thr Thr Asn Glu Arg Met Asn Ala Arg 545 550 555 560

Arg Tyr Lys His Phe Lys Val Thr Thr Thr Ser Ile Glu Ser Pro Phe 565 570 575

Asn His Gly Cys Val Arg Asn Ile Ile Asp Phe Phe Glu Phe Arg Cys
580 585 590

Cys Gly Leu Phe Arg Pro Val Ile Val Asp Trp Thr Arg Gln Tyr Thr
595 600 605

Ile Glu Tyr Asp Gln Ile Ser Gly Ser Gly Tyr Gln Leu Val
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<212> DNA

<213> Homo sapiens

<220>

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<400> 64

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Met Ala Asp Gly Pro Asp Glu Tyr Asp Thr Glu Ala

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ggc tgt gtg ccc ctt ctc cac cca gag gaa atc aaa ccc caa agc cat 97
Gly Cys Val Pro Leu Leu His Pro Glu Glu Ile Lys Pro Gln Ser His
15 20 25

tat aac cat gga tat ggt gaa cct ctt gga cgg aaa act cat att gat 145
Tyr Asn His Gly Tyr Gly Glu Pro Leu Gly Arg Lys Thr His Ile Asp
30 35 40

gat tac agc aca tgg gac ata gtc aag gct aca caa tat gga ata tat 193
Asp Tyr Ser Thr Trp Asp Ile Val Lys Ala Thr Gln Tyr Gly Ile Tyr
45 50 55 60

gaa cgc tgt cga gaa ttg gtg gaa gca ggt tat gat gta cgg caa ccg 241 Glu Arg Cys Arg Glu Leu Val Glu Ala Gly Tyr Asp Val Arg Gln Pro 65 70 75

gac aaa gaa aat gtt acc ctc ctc cat tgg gct gcc atc aat aac aga 289
Asp Lys Glu Asn Val Thr Leu Leu His Trp Ala Ala Ile Asn Asn Arg
80 85 90

ata gat tta gtc aaa tac tat att tcg aaa ggt gct att gtg gat caa 337

Ile Asp Leu Val Lys Tyr Tyr Ile Ser Lys Gly Ala Ile Val Asp Gln
95 100 105

ctt gga ggg gac ctg aat toa act coa ttg cac tgg gcc aca aga caa 385 Leu Gly Gly Asp Leu Asn Ser Thr Pro Leu His Trp Ala Thr Arg Gln 201/735

	110					115					120					
ggc	cat	cta	tee	atg	gtt	gtg	caa	cta	atg	aaa	tat	ggt.	gca	gat	cct	433
	His							_					_			100
125	1113	Dou	501	moo	130	,	0111	Dou	2.100	135	-,-	01,		пор	140	
125					150					100					140	
4	 .	_4.4							.		+		+			401
	tta															481
Ser	Leu	TTe	Asp		Glu	Gly	Cys	Ser		TTe	His	Leu	Ala		GIn	
				145					150					155		
ttc	gga	cat	acc	tca	att	gtt	gct	tat	ctc	ata	gca	aaa	gga	cag	gat	529
Phe	Gly	His	Thr	Ser	Ile	Val	Ala	Tyr	Leu	Ile	Ala	Lys	Gly	Gln	Aśp	
			160					165					170			
gta	gat	atg	atg	gat	cag	aat	gga	atg	acg	cct	tta	atg	tgg	gca	gca	577
Val	Asp	Met	Met	Asp	Gln	Asn	Gly	Met	Thr	Pro	Leu	Met	Trp	Ala	Ala	
		175					180					185				
tat	aga	aca	cat	agt	gtg	gat	cca	act	aga	ttg	ctt	tta	aca	ttc	aat	625
Tyr	Arg	Thr	His	Ser	Val	Asp	Pro	Thr	Arg	Leu	Leu	Leu	Thr	Phe	Asn	
•	190					195			_		200					
σt+	tca	σ++	990	ctt	aat	gar	ឧឧଟ	tat	cac	222	aac	act	gct.	ctg	cat	673
																0.0
	Ser	vai	ASII	Leu		Asp	Lys	I y I	nrs		ASII	Ш	МІА	Leu		
205					210					215					220	
																_
tgg	gca	gtg	cta	gca	ggg	aat	acc	aca	gtc	att	agc	ctt	ctt	ctg	gaa	721
Trp	Ala	Val	Leu	Ala	Gly	Asn	Thr	Thr	Val	Ile	${\tt Ser}$	Leu	Leu	Leu	Glu	

230

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235

225

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gct	gga	gct	aat	gtt	gat	gcc	cag	aat	atc	aag	ggc	gaa	tca	gcg	ctt	769
Ala	Gly	Ala	Asn	Val	Asp	Ala	Gln	Asn	Ile	Lys	Gly	Glu	Ser	Ala	Leu	
			240					245					250			
gat	ttg	gca	aaa	cag	aga	aaa	aat	gtg	tgg	atg	atc	aac	cac	tta	caa	817
Asp	Leu	Ala	Lys	Gln	Arg	Lys	Asn	Val	Trp	Met	Ile	Asn	His	Leu	Gln	
		255					260					265				
gag	gca	agg	caa	gca	aaa	gga	tat	gac	aat	ccg	tcc	ttc	ctt	aga	aag	865
Glu	Ala	Arg	Gln	Ala	Lys	Gly	Tyr	Asp	Asn	Pro	Ser	Phe	Leu	Arg	Lys	
	270					275					280					
ctg	aaa	gct	gat	aag	gaa	ttt	cgg	cag	aaa	gta	atg	tta	gga	act	cct	913
Leu	Lys	Ala	Asp	Lys	Glu	Phe	Arg	G1n	Lys	Val	Met	Leu	Gly	Thr	Pro	
285					290					295					300	
ttc	cta	gtt	att	tgg	ctg	gtt	ggg	ttt	ata	gca	gac	cta	aat	att	gat	961
Phe	Leu	Val	Ile	Trp	Leu	Val	Gly	Phe	Ile	Ala	Asp	Leu	Asn	Ile	Asp	
				305					310					315	-	
tct	tgg	ctc	att	aaa	ggg	cta	atg	tat	ggt	ggt	gtt	tgg	gct	aca	gta	1009
Ser	Trp	Leu	Ile	Lys	Gly	Leu	Met	Tyr	Gly	G1y	Val	Trp	Ala	Thr	Val	
			320					325					330			
cag	ttt	ctt	tca	aaa	tcc	ttt	ttc	gat	cat	tca	atg	cat	agt	gca	ttg	1057
Gln	Phe	Leu	Ser	Lys	Ser	Phe	Phe	Asp	His	Ser	Met	His	Ser	Ala	Leu	
		335					340					345				

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ccc	ctt	ggg	ata	tat	ttg	gca	acc	aaa	ttc	tgg	atg	tat	gtg	acg	tgg	1105
Pro	Leu	Gly	Ile	Tyr	Leu	Ala	Thr	Lys	Phe	Trp	Met	Tyr	Val	Thr	Trp	
	350					355					360				٠	
ttc	ttc	tgg	ttt	tgg	aat	gat	ctc	aac	ttt	tta	ttt	atc	cat	ctt	cca	1153
Phe	Phe	Trp	Phe	Trp	Asn	Asp	Leu	Asn	Phe	Leu	Phe	Ile	His	Leu	Pro	
365					370					375					380	
ttc	ctt	gcc	aat	agt	gtt	gca	ctt	ttc	tac	aat	ttt	gga	aaa	tct	tgg	1201
Phe	Leu	Ala	Asn	Ser	Val	Ala	Leu	Phe	Tyr	Asn	Phe	Gly	Lys	Ser	Trp	
				385					390					395		
aaa	tca	gat	cca	ggg	att	att	aaa	gca	aca	gaa	gag	caa	aag	aaa	aag	1249
Lys	Ser	Asp	Pro	Gly	Ile	Ile	Lys	Ala	Thr	Glu	Glu	Gln	Lys	Lys	Lys	
			400					405					410			
aca	ata	gtt	gaa	ctt	gca	gag	aca	gga	agt	ctg	gac	ctc	agt	ata	ttc	1297
Thr	Ile	Val	Glu	Leu	Ala	Glu	Thr	Gly	Ser	Leu	Asp	Leu	Ser	Ile	Phe	
		415					420					425				
tgc	agt	acc	tgt	ttg	ata	cga	aaa	ccg	gtg	agg	tcc	aaa	cat	tgt	ggt	1345
Cys	Ser	Thr	Cys	Leu	Ile	Arg	Lys	Pro	Val	Arg	Ser	Lys	His	Cys	G1y	
	430				-	435					440					
													cca			1393
Val	Cys	Asn ·	Arg	Cys		Ala	Lys	Phe	Asp		His	Cys	Pro	Trp	Val	
445					450					455					460	
															٠	
ggt	aac	tgt	gta	ggt	gca	ggc	aac	cat 204/		tat	ttt	atg	ggc	tac	cta	1441

Gly	Asn	Cys	Val	Gly	Ala	Gly	Asn	His	Arg	Tyr	Phe	Met	Gly	Tyr	Leu	
				465					470					475		
ttc	ttc	ttg	ctt	ttt	atg	atc	tgc	tgg	atg	att	tat	ggt	tgt	ata	tct	1489
Phe	Phe	Leu	Leu	Phe	Met	Ile	Cys	Trp	Met	Ile	Tyr	Gly	Cys	Ile	Ser	
			480					485					490			
tac	tgg	gga	ctc	cac	tgt	gag	acc	act	tac	acc	aag	gat	gga	ttt	tgg	1537
Tyr	Trp	Gly	Leu	His	Cys	Glu	Thr	Thr	Tyr	Thr	Lys	Asp	Gly	Phe	Trp	
		495					500					505			•	
aca	tac	att	act	cag	att	gcc	acg	tgt	tca	cct	tgg	atg	ttt	tgg	atg	1585
Thr	Tyr	Ile	Thr	G1n	Ile	Ala	Thr	Cys	Ser	Pro	Trp	Met	Phe	Trp	Met	
	510					515					520					
ttc	ctg	aac	agt	gtt	ttc	cac	ttc	atg	tgg	gtg	gct	gta	tta	ctc	atg	1633
Phe	Leu	Asn	Ser	Val	Phe	His	Phe	Met	Trp	Val	Ala	Val	Leu	Leu	Met	
525					530					535					540	
tgt	cag	atg	tac	cag	ata	tca	tgt	tta	ggt	att	act	aca	aat	gaa	aga	1681
Cys	G1n	Met	Tyr	G1n	Ile	Ser	Cys	Leu	Gly	Ile	Thr	Thr	Asn	Glu	Arg	•
				545					550					555		
atg	aat	gcc	agg	aga	tac	aag	cac	ttt	aaa	gtc	aca	aca	acg	tct	att	1729
Met	Asn	Ala	Arg	Arg	Tyr	Lys	His	Phe	Lys	Val	Thr	Thr	Thr	Ser	Ile	
			560					565					570			
gaa	agc	cca	ttc	aac	cat	gga	tgt	gta	aga	aat	att	ata	gac	ttc	ttt	1777
Glu	Ser	Pro	Phe	Asn	His	Gly	Cys	Val	Arg	Asn	Ile	Ile	Asp	Phe	Phe	
								205/	735							

575 580 585

gaa ttt cga tgc tgt ggc ctc ttt cgt cct gtt atc gtg gac tgg acc 1825 Glu Phe Arg Cys Cys Gly Leu Phe Arg Pro Val Ile Val Asp Trp Thr 590 595 600

agg cag tat aca ata gaa tat gac caa ata tca gga tct ggg tac cag 1873

Arg Gln Tyr Thr Ile Glu Tyr Asp Gln Ile Ser Gly Ser Gly Tyr Gln

605 610 615 620

ctg gtg tagcgacatc ttatcctatg aagcatattg ctgagtggtg cctgaaaatt 1929 Leu Val

gtgtctgtcc gtgtctttct cacactcgaa tccacatcct ttgaacaaga gcatgctatg 1989

tgtagggcta atggtgaatt ttacagtctt tttttcaaca cttttattaa caaaagtaaa 2049

catggacaga acacactgcc atttctggga agagtaaaga tgataaaaaa taattttaat 2109

ggttcttaat gtggaaattc acaacatact caacttttgg gttttgttct cacagtattt 2169

ttcacaaaaa aagggtaaac ttattctatt gacagacatg gtgtactgat cagaaatgtt 2229

cagttttaac taaaactaaa tttatgttat ttggctaaat gttatgatgc agtctagtac 2289

gagtattgca tctaattcca ggagcattgt tttaagttga ttgactagtt attatgtaca 2349

tttcagaatg tacacataaa tactgtgatg aaaatcatgt gattgggatc tactgtatg 2409

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ttttgttcaa atttaaaagc cctgctaatt gcatgacaca ccacatagaa tgtatactag 2649
cagatactat ccagtgaagc ataaattaga atttaatttg atgttcaaaa acagttccat 2709
ttttaagggt taaggtggta ttttcaagaa aaggcagaac aaataatgca aaattctcag 2769
taatagtgat acatggatat acttccttt aaattctcag ctgcaaaata attgtagaca 2829
aaataatggc atttaactaa agatggagca tgatctgtgt acatagcaca tgtgaataaa 2889
agaaaagctg acagtatatt ctggtttcaa taaaatgacc tatcagaaag tagaatttc 2948

<210> 65

<211> 632

<212> PRT

<213> Homo sapiens

<400> 65

Met Gln Arg Glu Glu Gly Phe Asn Thr Lys Met Ala Asp Gly Pro Asp

1 5 10 15

Glu Tyr Asp Thr Glu Ala Gly Cys Val Pro Leu Leu His Pro Glu Glu 207/735

WO 02/053737			PCT/JP01/11389
20	25	30	

Ile Lys Pro Gln Ser His Tyr Asn His Gly Tyr Gly Glu Pro Leu Gly
35 40 45

Arg Lys Thr His Ile Asp Asp Tyr Ser Thr Trp Asp Ile Val Lys Ala
50 55 60

Thr Gln Tyr Gly Ile Tyr Glu Arg Cys Arg Glu Leu Val Glu Ala Gly
65 70 75 80

Tyr Asp Val Arg Gln Pro Asp Lys Glu Asn Val Thr Leu Leu His Trp

85 90 95

Ala Ala Ile Asn Asn Arg Ile Asp Leu Val Lys Tyr Tyr Ile Ser Lys

100 105 110

Gly Ala Ile Val Asp Gln Leu Gly Gly Asp Leu Asn Ser Thr Pro Leu
115 120 125

His Trp Ala Thr Arg Gln Gly His Leu Ser Met Val Val Gln Leu Met 130 135 140

Lys Tyr Gly Ala Asp Pro Ser Leu Ile Asp Gly Glu Gly Cys Ser Cys 145 150 155 160

Ile His Leu Ala Ala Gln Phe Gly His Thr Ser Ile Val Ala Tyr Leu
165 170 175

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Ile	Ala	Lys	Gly 180	Gln	Asp	Val	Asp	Met 185	Met	Asp	Gln	Asn	Gly 190	Met	Thr
Pro	Leu	Met 195	Trp	Ala	Ala	Tyr	Arg 200	Thr	His	Ser	Val	Asp 205	Pro	Thr	Arg
Leu	Leu 210	Leu	Thr	Phe	Asn	Val 215	Ser	Val	Asn	Leu	Gly 220	Asp	Lys	Tyr	His
Lys 225	Asn	Thr	Ala	Leu	His 230	Trp	Ala	Val	Leu	Ala 235	G1y	Asn	Thr	Thr	Val 240
Ile	Ser	Leu	Leu	Leu 245	Glu	Ala	Gly	Ala	Asn 250	Val	Asp	Ala	G1n	Asn 255	Ile
Lys	Gly	Glu	Ser 260	Ala	Leu	Asp	Leu	Ala 265	Lys	G1n	Arg	Lys	Asn 270	Val	Trp
Met	Ile	Asn 275	His	Leu	Gln	Glu	Ala 280	Arg	Gln	Ala	Lys	G1y 285	Tyr	Asp	Asn
Pro	Ser 290	Phe	Leu	Arg	Lys	Leu 295	Lys	Ala	Asp	Lys	Glu 300	Phe	Arg	Gln	Lys
Val 305	Met	Leu	Gly	Thr	Pro 310	Phe	Leu	Val	Ile	Trp 315	Leu	Val	Gly	Phe	Ile 320

Ala Asp Leu Asn Ile Asp Ser Trp Leu Ile Lys Gly Leu Met Tyr Gly

325

330

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335

Gly Val Trp Ala Thr Val Gln Phe Leu Ser Lys Ser Phe Phe Asp His Ser Met His Ser Ala Leu Pro Leu Gly Ile Tyr Leu Ala Thr Lys Phe Trp Met Tyr Val Thr Trp Phe Phe Trp Phe Trp Asn Asp Leu Asn Phe Leu Phe Ile His Leu Pro Phe Leu Ala Asn Ser Val Ala Leu Phe Tyr Asn Phe Gly Lys Ser Trp Lys Ser Asp Pro Gly Ile Ile Lys Ala Thr Glu Glu Gln Lys Lys Lys Thr Ile Val Glu Leu Ala Glu Thr Gly Ser Leu Asp Leu Ser Ile Phe Cys Ser Thr Cys Leu Ile Arg Lys Pro Val Arg Ser Lys His Cys Gly Val Cys Asn Arg Cys Ile Ala Lys Phe Asp His His Cys Pro Trp Val Gly Asn Cys Val Gly Ala Gly Asn His Arg

Tyr Phe Met Gly Tyr Leu Phe Phe Leu Leu Phe Met Ile Cys Trp Met 210/735

485 490 495

Ile Tyr Gly Cys Ile Ser Tyr Trp Gly Leu His Cys Glu Thr Thr Tyr
500 505 510

Thr Lys Asp Gly Phe Trp Thr Tyr Ile Thr Gln Ile Ala Thr Cys Ser
515 520 525

Pro Trp Met Phe Trp Met Phe Leu Asn Ser Val Phe His Phe Met Trp
530 535 540

Val Ala Val Leu Leu Met Cys Gln Met Tyr Gln Ile Ser Cys Leu Gly 545 550 555 560

Ile Thr Thr Asn Glu Arg Met Asn Ala Arg Arg Tyr Lys His Phe Lys
565 570 575

Val Thr Thr Ser Ile Glu Ser Pro Phe Asn His Gly Cys Val Arg
580 585 590

Asn Ile Ile Asp Phe Phe Glu Phe Arg Cys Cys Gly Leu Phe Arg Pro
595 600 605

Val Ile Val Asp Trp Thr Arg Gln Tyr Thr Ile Glu Tyr Asp Gln Ile 610 615 620

Ser Gly Ser Gly Tyr Gln Leu Val 625 630

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<213> Homo sapiens

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<222> (108).. (2003)

<400> 66

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Met Gln Arg

1

50

gag gag gga ttt aac acc aag atg gcg gac ggc ccg gat gag tac gat 164
Glu Glu Gly Phe Asn Thr Lys Met Ala Asp Gly Pro Asp Glu Tyr Asp
5 10 15

acc gaa gcg ggc tgt gtg ccc ctt ctc cac cca gag gaa atc aaa ccc 212

Thr Glu Ala Gly Cys Val Pro Leu Leu His Pro Glu Glu Ile Lys Pro
20 25 30 35

caa agc cat tat aac cat gga tat ggt gaa cct ctt gga cgg aaa act 260 Gln Ser His Tyr Asn His Gly Tyr Gly Glu Pro Leu Gly Arg Lys Thr

40

45

WO 02/053737	PCT/JP01/11389

	cat	att	gat	gat	tac	agc	aca	tgg	gac	ata	gtc	aag	gct	aca	caa	tat	308
	His	Ile	Asp	Asp	Tyr	Ser	Thr	Trp	Asp	Ile	Val	Lys	Ala	Thr	Gln	Tyr	
				55					60					65			
	gga	ata	tat	gaa	cgc	tgt	cga	gaa	ttg	gtg	gaa	gca	ggt	tat	gat	gta	356
	Gly	Ile	Tyr	Glu	Arg	Cys	Arg	Glu	Leu	Val	Glu	Ala	Gly	Tyr	Asp	Val	
			70					75					80				
	cgg	caa	ccg	gac	aaa	gaa	aat	gtt	acc	ctc	ctc	cat	tgg	gct	gcc	atc	404
	Arg	Gln	Pro	Asp	Lys	Glu	Asn	Val	Thr	Leu	Leu	His	Trp	Ala	Ala	Ile	
		85					90					95					
	aat	aac	aga	ata	gat	tta	gtc	aaa	tac	tat	att	tcg	aaa	ggt	gct	att	452
	Asn	Asn	Arg	Ile	Asp	Leu	Val	Lys	Tyr	Tyr	Ile	Ser	Lys	G1y	Ala	Ile	
	100			•		105					110					115	
	gtg	gat	caa	ctt	gga	ggg	gac	ctg	aat	tca	act	cca	ttg	cac	tgg	gcc	500
	Val	Asp	G1n	Leu	Gly	Gly	Asp	Leu	Asn	Ser	Thr	Pro	Leu	His	Trp	Ala	
					120					125					130		
	aca	aga	caa	ggc	cat	cta	tcc	atg	gtt	gtg	caa	cta	atg	aaa	tat	ggt	548
		Arg															
				135					140					145			
														-			
	gca	gat	cct	tca	tta	att	gat	gga	gaa	gga	tgt	agc	tgt	att	cat	ctg	596
		Asp															-
•		-	150					155	- -	•	- , -		160				
	gct	gct	Cao	tte	gga	cat	acc	tos	att	g††	gc†	tat	ctc	at a	gra	ลลล	644
	g C C	got	vag		gga	cat	acc	cca	213/		дос	uau		ava	gca	aaa	044

Ala Ala Gln Phe Gly His Thr Ser Ile Val Ala Tyr Leu Ile Ala Lys

	165					170					175					
gga	cag	gat	gta	gat	atg	atg	gat	cag	aat	gga	atg	acg	cct	tta	atg	692
Gly	Gln	Asp	Val	Asp	Met	Met	Asp	Gln	Asn	Gly	Met	Thr	Pro	Leu	Met	
180					185					190					195	
															•	
tgg	gca	gca	tat	aga	aca	cat	agt	gtg	gat	cca	act	aga	ttg	ctt	tta	740
ſrp	Ala	Ala	Tyr	Arg	Thr	His	Ser	Val	Asp	Pro	Thr	Arg	Leu	Leu	Leu	
				200					205					210		
aca	ttc	aat	gtt	tca	gtt	aac	ctt	ggt	gac	aag	tat	cac	aaa	aac	act	788
Thr	Phe	Asn	Val	Ser	Val	Asn	Leu	Gly	qaA	Lys	Tyr	His	Lys	Asn	Thr	
			215					220					225			
gct	ctg	cat	tgg	gca	gtg	cta	gca	ggg	aat	acc	aca	gtc	att	agc	ctt	836
Ala	Leu	His	Trp	Ala	Val	Leu	Ala	Gly	Asn	Thr	Thr	Val	Ile	Ser	Leu	
		230					235					240				
ctt	ctg	gaa	gct	gga	gct	aat	gtt	gat	gcc	cag	aat	atc	aag	ggc	gaa	884
Leu	Leu	G1u	Ala	G1y	Ala	Asn	Val	Asp	Ala	G1n	Asn	Ile	Lys	Gly	Glu	
	245					250					255					
tca	gcg	ctt	gat	ttg	gca	aaa	cag	aga	aaa	aat	gtg	tgg	atg	atc	aac	932
Ser	Ala	Leu	Asp	Leu	Ala	Lys	G1n	Arg	Lys	Asn	Val	Trp	Met	Ile	Asn	
260					265					270					275	
cac	tta	caa	gag	gca	agg	caa	gca	aaa	gga	tat	gac	aat	ccg	tcc	ttc	980
His	Leu	Gln	G1u	Ala	Arg	Gln	Ala	Lys	G1y	Tyr	Asp	Asn	Pro	Ser	Phe	
								214/	735							

	-			280					285					290		
ctt	aga	aag	ctg	aaa	gct	gat	aag	gaa	ttt	cgg	cag	aaa	gta	atg	tta	1028
Leu	Arg	Lys	Leu	Lys	Ala	Asp	Lys	Glu	Phe	Arg	Gln	Lys	Val	Met	Leu	
			295					300					305			
gga	act	cct	ttc	cta	gtt	att	tgg	ctg	gtt	ggg	ttt	ata	gca	gac	cta	1076
Gly	Thr	Pro	Phe	Leu	Val	Ile	Trp	Leu	Val	Gly	Phe	Ile	Ala	Asp	Leu	
		310					315					320				
aat	att	gat	tct	tgg	ctc	att	aaa	ggg	cta	atg	tat	ggt	ggt	gtt	tgg	1124
Asn	Ile	Asp	Ser	Trp	Leu	Ile	Lys	Gly	Leu	Met	Tyr	Gly	Gly	Val	Trp	
	325					330					335					
gct	aca	gta	cag	ttt	ctt	tca	aaa	tcc	ttt	ttc	gat	cat	tca	atg	cat	1172
Ala	Thr	Val	Gln	Phe	Leu	Ser	Lys	Ser	Phe	Phe	Asp	His	Ser	Met	His	
340					345					350					355	
agt	gca	ttg	ccc	ctt	ggg	ata	tat	ttg	gca	acc	aaa	ttc	tgg	atg	tat	1220
Ser	Ala	Leu	Pro	Leu	Gly	Ile	Tyr	Leu	Ala	Thr	Lys	Phe	Trp	Met	Tyr	
				360					365					370		
gtg	acg	tgg	ttc	ttc	tgg	ttt	tgg	aat	gat	ctc	aac	ttt	tta	ttt	atc	1268
								Asn								
		-	375		-		_	380	-				385			
cat	ctt	cca	tte	ctt	gcc	aat	agt.	gtt	gca	ctt	ttc	tac	aat	ttt	gga	1316
								Val								
III	Lou	110	1 116	Luu	ura	non	JUI	141	1114	שטענ	1 116	1 y 1	non	1 116	JLY	

395

215/735

400

PCT/JP01/11389

WO 02/053737

390

aaa	tct	tgg	aaa	tca	gat	cca	ggg	att	att	aaa	gca	aca	gaa	gag	caa	1364
Lys	Ser	Trp	Lys	Ser	Asp	Pro	Gly	Ile	Ile	Lys	Ala	Thr	Glu	Glu	G1n	
	405					410					415					
aag	aaa	aag	aca	ata	gtt	gaa	ctt	gca	gag	aca	gga	agt	ctg	gac	ctc	1412
Lys	Lys	Lys	Thr	Ile	Val	G1u	Leu	Ala	Glu	Thr	Gly	Ser	Leu	Asp	Leu	
420					425					430					435	
agt	ata	ttc	tgc	agt	acc	tgt	ttg	ata	cga	aaa	ccg	gtg	agg	tcc	aaa	1460
Ser	Ile	Phe	Cys	Ser	Thr	Cys	Leu	Ile	Arg	Lys	Pro	Val	Arg	Ser	Lys	
				440					445					450		
cat	tgt	ggt	gtg	tgc	aac	cgc	tgt	ata	gca	aaa	ttt	gat	cat	cat	tgc	1508
His	Cys	Gly	Val	Cys	Asn	Arg	Cys	Ile	Ala	Lys	Phe	Asp	His	His	Cys	
			455					460					465			
cca	tgg	gtg	ggt	aac	tgt	gta	ggt	gca	ggc	aac	cat	aga	tat	ttt	atg	1556
Pro	Trp	Val	Gly	Asn	Cys	Val	Gly	Ala	G1y	Asn	His	Arg	Tyr	Phe	Met	
		470					475					480				
ggc	tac	cta	ttc	ttc	ttg	ctt	ttt	atg	atc	tgc	tgg	atg	att	tat	ggt	1604
Gly	Tyr	Leu	Phe	Phe	Leu	Leu	Phe	Met	Ile	Cys	Trp	Met	Ile	Tyr	Gly	
	485					490					495					
tgt	ata	tct	tac	tgg	gga	ctc	cac	tgt	gag	acc	act	tac	acc	aag	gat	1652
Cys	Ile	Ser	Tyr	Trp	Gly	Leu	His	Cys	Glu	Thr	Thr	Tyr	Thr	Lys	Asp	
500					505					510					515	
					•											

gga	ttt	tgg	aca	tac	att	act	cag	att	gcc	acg	tgt	tca	cct	tgg	atg	1700
Gly	Phe	Trp	Thr	Tyr	Ile	Thr	Gln	Ile	Ala	Thr	Cys	Ser	Pro	Trp	Met	
				520					525					530	•	
ttt	tgg	atg	ttc	ctg	aac	agt	gtt	ttc	cac	ttc	atg	tgg	gtg	gct	gta	1748
Phe	Trp	Met	Phe	Leu	Asn	Ser	Val	Phe	His	Phe	Met	Trp	Val	Ala	Val	
			535					540					545			
tta	ctc	atg	tgt	cag	atg	tac	cag	ata	tca	tgt	tta	ggt	att	act	aca	1796
Leu	Leu	Met	Cys	Gln	Met	Tyr	G1n	Ile	Ser	Cys	Leu	G1y	Ile	Thr	Thr	
		550					555					560				
aat	gaa	aga	atg	aat	gcc	agg	aga	tac	aag	cac	ttt	aaa	gtc	aca	aca	1844
Asn	Glu	Arg	Met	Asn	Ala	Arg	Arg	Tyr	Lys	His	Phe	Lys	Val	Thr	Thr	
	565					570					575					
															•	
acg	tct	att	gaa	agc	cca	ttc	aac	cat	gga	tgt	gta	aga	aat	att	ata	1892
Thr	Ser	Ile	G1u	Ser	Pro	Phe	Asn	His	Gly	Cys	Val	Arg	Asn	Ile	Ile	
580					585					590					595	
gac	ttc	ttt	gaa	ttt	cga	tgc	tgt	ggc	ctc	ttt	cgt	cct	gtt	atc	gtg	1940
Asp	Phe	Phe	Glu	Phe	Arg	Cys	Cys	Gly	Leu	Phe	Arg	Pro	Val	Ile	Val	
				600					605					610		
gac	tgg	acc	agg	cag	tat	aca	ata	gaa	tat	gac	caa	ata	tca	gga	tct	1988
Asp	Trp	Thr	Arg	G1n	Tyr	Thr	Ile	G1u	Tyr	Asp	G1n	Ile	Ser	Gly	Ser	
			615					620					625			
ggg	tac	cag	ctg	gtg	tago	gaca	atc 1			tg as	agcat	tatte	g ctg	gagte	ggtg	2043
								217/	735							

Gly Tyr Gln Leu Val

630

cctgaaaatt gtgtctgtcc gtgtctttct cacactcgaa tccacatcct ttgaacaaga 2103 gcatgctatg tgtagggcta atggtgaatt ttacagtctt tttttcaaca cttttattaa 2163 caaaagtaaa catggacaga acacactgcc atttctggga agagtaaaga tgataaaaaa 2223 taattttaat ggttcttaat gtggaaattc acaacatact caacttttgg gttttgttct 2283 cacagtattt ttcacaaaaa aagggtaaac ttattctatt gacagacatg gtgtactgat 2343 cagaaatgtt cagttttaac taaaactaaa tttatgttat ttggctaaat gttatgatgc 2403 agtctagtac gagtattgca tctaattcca ggagcattgt tttaagttga ttgactagtt 2463 attatgtaca tttcagaatg tacacataaa tactgtgatg aaaatcatgt gattgggatc 2523 tactgtgatg ttgtcttcaa aggcaggaga aaataatgtt cacaataaaa tgtgctaaca 2583 atgttttgtt tctatcagct gttgcaatgc tgatatattt ctagttcagt gaaataattt 2643 gtagtaacct tactctgagg ttttacggtc tgataatgaa gcacttgcat gagtatagta 2703 agtcatgttt ttttgttcaa atttaaaagc cctgctaatt gcatgacaca ccacatagaa 2763 tgtatactag cagatactat ccagtgaagc ataaattaga atttaatttg atgttcaaaa 2823

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ataagtcaca catcaaaaaa agattaccct tagtgtatgt gttttaatat tagaaaattg 3783 gcatatgtac tttatttttg aaaagggaag agatgggtgt ggggtggcaa tagcattgtg 3843 ccattttgtc atagaatgta aaaattggtt aactttacaa atgtcagcta gttttgacta 3903 ctaattgggg gaaattttag ataattttta aattcaaagt tatttataaa atgctagaat 3963 ttgttttaat tttttgtatt ttgagccact tcacatgaag actcagttgc atttttatcg 4023 aatacatttt tatcaacagt taaagactat ggtggttttt tcagagtttg gctaagaatg 4083 ttgttaccat cttctttgtt tgtggtacaa tattttcagt gcaaaagaga tgtcattcag 4143 ttaaaaagac aaacctctag atgtgtaatt acatggaaaa tactagcaat gtgaatgctt 4203 ttgtagtaac catcttgtag tacctgtgaa atctataact cagaaatggt cagatggtca 4263 ggagccagct atgcagcagt ataccatctg tttaattatt ttgtaggtcc tgtgtgtgga 4323 accaactata aacccagttc taaagttgtg tatgatggtg aacctttggg aatagttctt 4383 atcaacttaa ttggatactt ttagcaaata ggaacttaat tctcagcact gaacatgaat 4443 tacttccttg gagttttttt tcattcatat ttttgttgtt tccaggaatt tatttgatat 4503 taatgggcgt aaaacagcat cattgtactt aagctatgga tgtttttatt ttatattttc 4563

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4715

<210> 67

<211> 498

<212> PRT

<213> Homo sapiens

<400> 67

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Leu Val Ser Pro Asn Ser Ser His Ser His Ala Val Val Leu Ser Trp
20 25 30

Val Arg Pro Phe Asp Gly Asn Ser Pro Ile Leu Tyr Tyr Ile Val Glu 35 40 45

Leu Ser Glu Asn Asn Ser Pro Trp Lys Val His Leu Ser Asn Val Gly
50 55 60

Pro Glu Met Thr Gly Val Thr Val Ser Gly Leu Thr Pro Ala Arg Thr
65 70 75 80

Tyr Gln Phe Arg Val Cys Ala Val Asn Glu Val Gly Arg Gly Gln Tyr 221/735

W	O 02/	05373	3 7												PCT/JP01/11389
				85					90					95	
Ser	Ala	G1u	Thr 100	Ser	Arg	Leu	Met	Leu 105	Pro	Glu	Glu	Pro	Pro 110	Ser	Ala
Pro	Pro	Lys 115	Asn	Ile	Val	Ala	Ser 120	Gly	Arg	Thr	Asn	Gln 125	Ser	Ile	Met
Val	Gln 130	Trp	Gln	Pro	Pro	Pro 135	Glu	Thr	Glu	His	Asn 140	Gly	Val	Leu	Arg
Gly 145	Tyr	Ile	Leu	Arg	Tyr 150	Arg	Leu	Ala	G1y	Leu 155	Pro	Gly	G1u	Tyr	Gln 160
Gln	Arg	Asn	Ile	Thr 165	Ser	Pro	Glu	Val	Asn 170	Tyr	Cys	Leu	Val	Thr 175	Asp
Leu	Ile	Ile	Trp 180	Thr	Gln	Tyr	G1u	Ile 185	Gln	Val	Ala	Ala	Tyr 190	Asn	Gly
Ala	G1y	Leu 195	Gly	Val	Phe	Ser	Arg 200	Ala	Val	Thr	Glu	Tyr 205	Thr	Leu	Gln

Ser Thr Thr Ile Gln Phe Leu Trp Asn Pro Pro Pro Gln Gln Phe Ile
225 230 235 240

Gly Val Pro Thr Ala Pro Pro Gln Asn Val Gln Thr Glu Ala Val Asn

215

210

220

Asn	Gly	Ile	Asn	Gln	Gly	Tyr	Lys	Leu	Leu	Ala	Trp	Pro	Ala	Asp	Ala
				245					250					255	
Pro	Glu	Ala	Val	Thr	Val	Val	Thr	Ile	Ala	Pro	Asp	Phe	His	Gly	Val
			260					265					270		
His	His	G1v	His	Ile	Thr	Asn	Leu	Lvs	Lvs	Phe	Thr	Ala	Tvr	Phe	Thr
		275					280	_,_	_,_			285	-,-		
		210					200					200			
_			_				_				_	_	_		_
Ser	Val	Leu	Cys	Phe	Thr	Thr	Pro	Gly	Asp	Gly	Pro	Pro	Ser	Thr	Pro
	290					295					300				
Gln	Leu	Val	Trp	Thr	G1n	Glu	Asp	Lys	Pro	Gly	Ala	Val	Gly	His	Leu
305					310					315					320
Ser	Phe	Thr	Glu	Ile	Leu	Asp	Thr	Ser	Leu	Lys	Val	Ser	Trp	Gln	Glu
				325					330					335	
				. – •											
D	T -45	C1.	Y	A	C1	71.	т1.	TL.	C1	Т	C1-	T1.	C	Т	C1
rro	∟eu	ΩTΠ	Lys	ASII	ΩŢΆ	TTG	116	1III	OTA	ıyr	an	TIG	ser	ırp	atn

Val Tyr Gly Arg Asn Asp Ser Arg Leu Thr His Thr Leu Asn Ser Thr

345

350

340

355 360 365

Met His Glu Tyr Lys Ile Gln Gly Leu Ser Ser Leu Thr Thr Tyr Thr 370 375 380

Ile Asp Val Ala Ala Val Thr Ala Val Gly Thr Gly Leu Val Thr Ser 385 390 390 395 400

Ser Thr Ile Ser Ser Gly Val Pro Pro Asp Leu Pro Gly Ala Pro Ser 405 410 415

Asn Leu Val Ile Ser Asn Ile Ser Pro Arg Ser Ala Thr Leu Gln Phe
420 425 430

Arg Pro Gly Tyr Asp Gly Lys Thr Ser Ile Ser Arg Trp Ile Val Glu
435 440 445

Gly Gln Met Arg Pro Glu Gly Val Gly Leu Pro Ala Glu Val Thr Gln
450 455 460

Pro Ser His Glu Ala Gly Leu Glu Pro Ala Asn Leu Gly Ser Leu Trp 465 470 475 480

Leu Leu Ser Leu Val Tyr Trp Cys Tyr Ser Gln Lys Leu Trp Glu Phe
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Ser Cys

<210> 68

<211> 1902

<212> DNA

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224/735

<221> CDS

<222> (22).. (1515)

<400> 68

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Met Ala Arg Leu Glu Val Ile Glu Leu Pro

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5 10

cat toa cot cag aac oto ctg gto ago cot aat tot too cac ago cac 99
His Ser Pro Gln Asn Leu Leu Val Ser Pro Asn Ser Ser His Ser His
15 20 25

gcc gtg gtg ctc tct tgg gtc cgg ccc ttt gat gga aac agt cct att 147
Ala Val Val Leu Ser Trp Val Arg Pro Phe Asp Gly Asn Ser Pro Ile
30 35 40

ctt tat tac atc gtg gag ctg tct gaa aac aac tct cca tgg aag gtg 195
Leu Tyr Tyr Ile Val Glu Leu Ser Glu Asn Asn Ser Pro Trp Lys Val
45 50 55

cat ctg tca aac gtt ggc cct gag atg aca ggc gtc acc gtg agt ggc 243
His Leu Ser Asn Val Gly Pro Glu Met Thr Gly Val Thr Val Ser Gly
60 65 70

ctg act ccg gct cgt acc tat caa ttc cgg gtg tgc gcg gtg aat gaa 291
Leu Thr Pro Ala Arg Thr Tyr Gln Phe Arg Val Cys Ala Val Asn Glu
75 80 85 90

gtg ggc agg ggc cag tac agt gcc gag aca agc agg ttg atg cta cct 339 225/735

Val	Gly	Arg	Gly	Gln	Tyr	Ser	Ala	Glu	Thr	Ser	Arg	Leu	Met	Leu	Pro	
				95					100					105		
gaa	gaa	cca	ссс	agt	gct	ссс	ccg	aaa	aat	ata	gtg	gcc	agt	ggg	cgg	387
Glu	Glu	Pro	Pro	Ser	Ala	Pro	Pro	Lys	Asn	Ile	Val	Ala	Ser	Gly	Arg	
			110					115					120			
act	aat	cag	tcc	att	atg	gtc	cag	tgg	cag	cca	ccc	cca	gaa	aca	gag	435
Thr	Asn	Gln	Ser	Ile	Met	Val	Gln	Trp	Gln	Pro	Pro	Pro	Glu	Thr	Glu	
		125					130					135				
															•	
cac	aac	ggg	gtg	ttg	cgt	gga	tac	atc	ctc	agg	tac	cgc	ctg	gct	ggc	483
His	Asn	Gly	Val	Leu	Arg	Gly	Tyr	Ile	Leu	Arg	Tyr	Arg	Leu	Ala	Gly	
	140					145					150					
ctt	ссс	gga	gag	tac	cag	cag	cgg	aac	atc	acc	agc	ccg	gag	gtg	aac	531
Leu	Pro	Gly	Glu	Tyr	Gln	Gln	Arg	Asn	Ile	Thr	Ser	Pro	Glu	Val	Asn	
155					160					165					170	
tac	tgc	ctg	gtg	aca	gac	ctg	atc	atc	tgg	aca	cag	tat	gag	ata	cag	579
Tyr	Cys	Leu	Val	Thr	Asp	Leu	Ile	Ile	Trp	Thr	Gln	Tyr	Glu	Ile	G1n	
				175					180					185		
gtg	gcg	gcg	tac	aac	ggg	gcc	ggt	ctg	ggc	gtc	ttc	agc	agg	gca	gtg	627
Val	Ala	Ala	Tyr	Asn	Gly	Ala	Gly	Leu	Gly	Val	Phe	Ser	Arg	Ala	Val	
			190					195					200			
								ccc								675
Thr	Glu	Tyr	Thr	Leu	Gln	Gly	Val	Pro		Ala	Pro	Pro	G1n	Asn	Val	
								226/	133							

		205		•			210					215				
cag	acg	gaa	gcc	gtg	aac	tcc	acc	acc	att	cag	ttc	ctg	tgg	aac	cct	723
								Thr								
	220		•			225					230					
ccg	cct	cag	cag	ttt	atc	aat	ggc	atc	aac	cag	gga	tac	aag	ctt	ctg	771
Pro	Pro	Gln	Gln	Phe	Ile	Asn	Gly	Ile	Asn	Gln	Gly	Tyr	Lys	Leu	Leu	
235					240					245					250	
gca	tgg	ccg	gca	gat	gcc	ccc	gag	gct	gtc	act	gtg	gtc	act	att	gcc	819
Ala	Trp	Pro	Ala	Asp	Ala	Pro	G1u	Ala	Val	Thr	Val	Val	Thr	Ile	Ala	
				255					260					265		
cca	gat	ttc	cac	gga	gtc	cac	cat	gga	cac	ata	acg	aac	ctg	aag	aag	867
Pro	Asp	Phe	His	G1y	Val	His	His	Gly	His	Ile	Thr	Asn	Leu	Lys	Lys	
			270					275					280			
ttt	acc	gcc	tac	ttc	act	tcc	gtt	ctg	tgc	ttc	acc	acc	cct	ggg	gac	915
Phe	Thr	Ala	Tyr	Phe	Thr	Ser	Val	Leu	Cys	Phe	Thr	Thr	Pro	Gly	Asp	
		285					290					295				
ggg	cct	ccc	agc	aca	cct	cag	ctg	gtc	tgg	act	cag	gaa	gac	aaa	cca	963
Gly	Pro	Pro	Ser	Thr	Pro	G1n	Leu	Val	Trp	Thr	Gln	G1u	Asp	Lys	Pro	
	300					305					310					
gga	gct	gtg	gga	cat	ctg	agt	ttc	aca	gag	atc	ttg	gac	aca	tct	ctc	1011
Gly	Ala	Val	Gly	His	Leu	Ser	Phe	Thr	G1u	Ile	Leu	Asp	Thr	Ser	Leu	
315					320					325					330	

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aag	gtc	agc	tgg	cag	gag	ccc	ctg	gag	aaa	aat	ggc	atc	att	act	ggc	1059
Lys	Val	Ser	Trp	Gln	Glu	Pro	Leu	Glu	Lys	Asn	Gly	Ile	Ile	Thr	Gly	
				335					340					345		
tat	cag	atc	tct	tgg	gaa	gtg	tac	ggc	agg	aac	gac	tct	cgt	ctc	acg	1107
Tyr	G1n	Ile	Ser	Trp	Glu	Val	Tyr	Gly	Arg	Asn	Asp	Ser	Arg	Leu	Thr	
			350					355					360			
cac	acc	ctg	aac	agc	acg	atg	cac	gag	tac	aag	atc	caa	ggc	ctc	tca	1155
His	Thr	Leu	Asn	Ser	Thr	Met	His	G1u	Tyr	Lys	Ile	Gln	Gly	Leu	Ser	
		365					370					375				
tct	ctc	acc	acc	tac	acc	atc	gac	gtg	gcc	gct	gtg	act	gcc	gtg	ggc	1203
Ser	Leu	Thr	Thr	Tyr	Thr	Ile	Asp	Val	Ala	Ala	Val	Thr	Ala	Val	Gly	
	380					385					390					
act	ggc	ctg	gtg	act	tca	tcc	acc	att	tct	tct	gga	gtg	ccc	cca	gac	1251
Thr	Gly	Leu	Val	Thr	Ser	Ser	Thr	Ile	Ser	Ser	G1y	Val	Pro	Pro	Asp	
395					400					405					410	
ctt	cct	ggt	gcc	cca	tcc	aac	ctg	gtc	att	tcc	aac	atc	agc	cct	cgc	1299
Leu	Pro	G1y	Ala	Pro	Ser	Asn	Leu	Val	Ile	Ser	Asn	Ile	Ser	Pro	Arg	
				415					420					425		
tcc	gcc	acc	ctt	cag	ttc	cgg	cca	ggc	tat	gac	ggg	aaa	acg	tcc	atc	1347
Ser	Ala	Thr	Leu	Gln	Phe	Arg	Pro	Gly	Tyr	Asp	G1y	Lys	Thr	Ser	Ile	
			430					435					440			

tcc agg tgg att gtt gag ggg cag atg aga cct gaa ggt gtt gga tta 1395
Ser Arg Trp Ile Val Glu Gly Gln Met Arg Pro Glu Gly Val Gly Leu
445 450 455

cct gcc gag gtc aca cag cca agc cat gaa gcc gga ttg gag cct gca 1443
Pro Ala Glu Val Thr Gln Pro Ser His Glu Ala Gly Leu Glu Pro Ala
460 465 470

aac ctc gga agt ctg tgg ctg ctc agc ctg gtg tat tgg tgt tac agc 1491

Asn Leu Gly Ser Leu Trp Leu Leu Ser Leu Val Tyr Trp Cys Tyr Ser

475 480 485 490

cag aaa ctt tgg gaa ttc tct tgt tagttggtta gttttactgt aattttctat 1545 Gln Lys Leu Trp Glu Phe Ser Cys

495

aaagaattea tateatetgt taatggegae agtttttgtt tetteetttg aatttttat 1605
attettett tetettttt gtttettett etttgagtat tttgtaatet taetgggagg 1665
getaaagegt ettetateat ategaattgg gacaatgata gaagacaate tttgttttgt 1725
cactetaaag aaattattgt aagattttat eateaggtat gacatttaea eeattgatgt 1785
aggetttta aaaaatatat eeageetgta ttgggttaag atgattett tetgateetg 1845
attteetagg agttggtttt tttttttta aageataaat aaatttaatt geateag 1902

<210> 69

<211> 498

<212> PRT

<213> Homo sapiens

<400> 69

Met Ala Arg Leu Glu Val Ile Glu Leu Pro His Ser Pro Gln Asn Leu

1 5 10 15

Leu Val Ser Pro Asn Ser Ser His Ser His Ala Val Val Leu Ser Trp
20 25 30

Val Arg Pro Phe Asp Gly Asn Ser Pro IIe Leu Tyr Tyr Ile Val Glu 35 40 45

Leu Ser Glu Asn Asn Ser Pro Trp Lys Val His Leu Ser Asn Val Gly
50 55 60

Pro Glu Met Thr Gly Val Thr Val Ser Gly Leu Thr Pro Ala Arg Thr
65 70 75 80

Tyr Gln Phe Arg Val Cys Ala Val Asn Glu Val Gly Arg Gly Gln Tyr 85 90 95

Ser Ala Glu Thr Ser Arg Leu Met Leu Pro Glu Glu Pro Pro Ser Ala 100 105 110

Pro Pro Lys Asn Ile Val Ala Ser Gly Arg Thr Asn Gln Ser Ile Met

115
120
125
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Val	Gln	Trp	Gln	Pro	Pro	Pro	Glu	Thr	Glu	His	Asn	Gly	Val	Leu	Arg
	130					135					140				
Gly	Tyr	Ile	Leu	Arg	Tyr	Arg	Leu	Ala	Gly	Leu	Pro	Gly	Glu	Tyr	Gln
145					150					155					160
Gln	Arg	Asn	Ile	Thr	Ser	Pro	Glu	Val	Asn	Tyr	Cys	Leu	Val	Thr	Asp
				165					170					175	
Leu	Ile	Ile	Trp	Thr	Gln	Tyr	Glu	Ile	Gln	Val	Ala	Ala	Tyr	Asn	Gly
			180					185					190		
Ala	G1y	Leu	Gly	Val	Phe	Ser	Arg	Ala	Val	Thr	G1u	Tyr	Thr	Leu	Gln
		195					200					205			
G1 y	Val	Pro	Thr	Ala	Pro	Pro	G1n	Asn	Val	G1n	Thr	G1u	Ala	Val	Asn
	210					215					220				
Ser	Thr	Thr	Ile	G1n	Phe	Leu	Trp	Asn	Pro	Pro	Pro	Gln	Gln	Phe	Ile
225					230					235					240
Asn	Gl v	Tle	Asn	Gl n	Glv	Tvr	Lvs	Leu	I.eu	Ala	Trn	Pro	Ala	Asn	Ala
11011	01,	-10		245	01,	.,.	2,3	Lou	250		p	110	u	255	1114
Dwa	C1	۸۱۵	Vol	The	Vol	Vol.	Th.	T1 a	41 a	Dwo	Aan	Dho	u: _	C1	V-1
LLO	GIU	utg	260	1111.	۷dl	Val	1111	265	wta	L1.0	usb	Phe	270	ату	AST
•••							_								
His	His	Gly	His	lle	Thr	Asn	Leu	Lys 231/		Phe	Thr	Ala	Tyr	Phe	Thr

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275 280 285

Ser Val Leu Cys Phe Thr Thr Pro Gly Asp Gly Pro Pro Ser Thr Pro 290 295 300

Gln Leu Val Trp Thr Gln Glu Asp Lys Pro Gly Ala Val Gly His Leu 305 310 315 320

Ser Phe Thr Glu Ile Leu Asp Thr Ser Leu Lys Val Ser Trp Gln Glu 325 330 335

Pro Leu Glu Lys Asn Gly Ile Ile Thr Gly Tyr Gln Ile Ser Trp Glu 340 345 350

Val Tyr Gly Arg Asn Asp Ser Arg Leu Thr His Thr Leu Asn Ser Thr 355 360 365

Thr His Glu Tyr Lys Ile Gln Gly Leu Ser Ser Leu Thr Thr Tyr Thr 370 375 380

Ile Asp Val Ala Ala Val Thr Ala Val Gly Thr Gly Leu Val Thr Ser 385 390 395 400

Ser Thr Ile Ser Ser Gly Val Pro Pro Asp Leu Pro Gly Ala Pro Ser
405 410 415

Asn Leu Val Ile Ser Asn Ile Ser Pro Arg Ser Ala Thr Leu Gln Phe
420 425 430

Arg Pro Gly Tyr Asp Gly Lys Thr Ser Ile Ser Arg Trp Ile Val Glu
435 440 445

Gly Gln Met Arg His Gln Gly Val Gly Leu Pro Ala Glu Val Thr Gln 450 455 460

Pro Ser His Glu Ala Gly Leu Glu Pro Ala Asn Leu Gly Ser Leu Trp
465 470 475 480

Leu Leu Ser Leu Val Tyr Trp Cys Tyr Ser Gln Lys Leu Trp Glu Phe
485 490 495

Ser Cys

<210> 70

<211> 1902

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (22).. (1515)

<400> 70

gaaggaggga atgactccag g atg gcc cgg ctg gaa gtg att gaa ctg cct 51

Met Ala Arg Leu Glu Val Ile Glu Leu Pro

1 5 10 233/735

cat	tca	cct	cag	aac	ctc	ctg	gtc	agc	cct	aat	tct	tcc	cac	agc	cac	99
His	Ser	Pro	Gln	Asn	Leu	Leu	Val	Ser	Pro	Asn	Ser	Ser	His	Ser	His	
				15					20					25		
gcc	gtg	gtg	ctc	tct	tgg	gtc	cgg	ccc	ttt	gat	gga	aac	agt	cct	att	147
Ala	Val	Val	Leu	Ser	Trp	Val	Arg	Pro	Phe	Asp	Gly	Asn	Ser	Pro	Ile	
			30					35					40			
ctt	tat	tac	atc	gtg	gag	ctg	tct	gaa	aac	aac	tct	cca	tgg	aag	gtg	195
Leu	Tyr	Tyr	Ile	Val	Glu	Leu	Ser	Glu	Asn	Asn	Ser	Pro	Trp	Lys	Val	
		4 5					50					55				
cat	ctg	tca	aac	gtt	ggc	cct	gag	atg	aca	ggc	gtc	acc	gtg	agt	ggc	243
His	Leu	Ser	Asn	Val	Gly	Pro	Glu	Met	Thr	Gly	Val	Thr	Val	Ser	Gly	
	60					65					70					
ctg	act	ccg	gct	cgt	acc	tat	caa	ttc	cgg	gtg	tgc	gcg	gtg	aat	gaa	291
Leu	Thr	Pro	Ala	Arg	Thr	Tyr	Gln	Phe	Arg	Val	Cys	Ala	Val	Asn	Glu	
75					80					85					90	
gtg	ggc	agg	ggc	cag	tac	agt	gcc	gag	aca	agc	agg	ttg	atg	cta	cct	339
Val	Gly	Arg	Gly	G1n	Tyr	Ser	Ala	Glu	Thr	Ser	Arg	Leu	Met	Leu	Pro	
				95					100					105		
gaa	gaa	cca	ccc	agt	gct	ccc	ccg	aaa	aat	ata	gtg	gcc	agt	ggg	cgg	387
Glu	Glu	Pro		Ser	Ala	Pro	Pro	Lys	Asn	Ile	Val	Ala	Ser	Gly	Arg	
			110					115					120			

act	aat	cag	tcc	att	atg	gtc	cag	tgg	cag	cca	ccc	cca	gaa	aca	gag	435
Thr	Asn	Gln	Ser	Ile	Met	Val	Gln	Trp	Gln	Pro	Pro	Pro	Glu	Thr	Glu	
		125					130					135				
cac	aac	ggg	gtg	ttg	cgt	gga	tac	atc	ctc	agg	tac	cgc	ctg	gct	ggc	483
His	Asn	Gly	Val	Leu	Arg	Gly	Tyr	Ile	Leu	Arg	Tyr	Arg	Leu	Ala	Gly	
	140					145					150					
ctt	ссс	gga	gag	tac	cag	cag	cgg	aac	atc	acc	agc	ccg	gag	gtg	aac	531
Leu	Pro	Gly	Glu	Tyr	Gln	Gln	Arg	Asn	Ile	Thr	Ser	Pro	G1u	Val	Asn	
155					160					165					170	
tac	tgc	ctg	gtg	aca	gac	ctg	atc	atc	tgg	aca	cag	tat	gag	ata	cag	579
Tyr	Cys	Leu	Val	Thr	Asp	Leu	Ile	Ile	Trp	Thr	G1n	Tyr	Glu	Ile	Gln	
				175					180					185		
		•														
gtg	gcg	gcg	tac	aac	ggg	gcc	ggt	ctg	ggc	gtc	ttc	agc	agg	gca	gtg	627
Val	Ala	Ala	Tyr	Asn	Gly	Ala	Gly	Leu	Gly	Val	Phe	Ser	Arg	Ala	Val	
			190					195					200			
acc	gag	tac	acc	ttg	cag	gga	gtg	ссс	acc	gcg	ccc	ccg	cag	aac	gtg	675
Thr	Glu	Tyr	Thr	Leu	G1n	Gly	Val	Pro	Thr	Ala	Pro	Pro	Gln	Asn	Val	
		205					210					215				
cag	acg	gaa	gcc	gtg	aac	tcc	acc	acc	att	cag	ttc	ctg	tgg	aac	cct	723
G1n	Thr	Glu	Ala	Val	Asn	Ser	Thr	Thr	Ile	Gln	Phe	Leu	Trp	Asn	Pro	
	220					225					230					
ccg	cct	cag	cag	ttt	atc	aat	ggc	atc	aac	cag	gga	tac	aag	ctt	ctg	771
								235/	735							

Pro	Pro	Gln	Gln	Phe	lle	Asn	Gly	TTe	Asn	GIn	Gly	Tyr	Lys	Leu	Leu	
235					240					245					250	
gca	tgg	ccg	gca	gat	gcc	ccc	gag	gct	gtc	act	gtg	gtc	act	att	gcc	819
Ala	Trp	Pro	Ala	Asp	Ala	Pro	Glu	Ala	Val	Thr	Val	Val	Thr	Ile	Ala	
				255					260					265		
cca	gat	ttc	cac	gga	gtc	cac	cat	gga	cac	ata	acg	aac	ctg	aag	aag	867
Pro	Asp	Phe	His	Gly	Val	His	His	Gly	His	Ile	Thr	Asn	Leu	Lys	Lys	
			270				1	275					280			
ttt	acc	gcc	tac	ttc	act	tcc	gtt	ctg	tgc	ttc	acc	acc	cct	ggg	gac	915
Phe	Thr	Ala	Tyr	Phe	Thr	Ser	Val	Leu	Cys	Phe	Thr	Thr	Pro	Gly	Asp	
		285					290					295				
ggg	cct	ccc	agc	aca	cct	cag	ctg	gtc	tgg	act	cag	gaa	gac	aaa	cca	963
Gly	Pro	Pro	Ser	Thr	Pro	Gln	Leu	Val	Trp	Thr	Gln	Glu	Asp	Lys	Pro	
	300					305					310					
gga	gct	gtg	gga	cat	ctg	agt	ttc	aca	gag	atc	ttg	gac	aca	tct	ctc	1011
Gly	Ala	Val	Gly	His	Leu	Ser	Phe	Thr	Glu	Ile	Leu	Asp	Thr	Ser	Leu	
315					320					325					330	
aag	gtc	agc	tgg	cag	gag	ccc	ctg	gag	aaa	aat	ggc	atc	att	act	ggc	1059
Lys	Val	Ser	Trp	Gln	Glu	Pro	Leu	Glu	Lys	Asn	Gly	Ile	Ile	Thr	Gly	
				335					340					345	٠	
tat	cag	atc	tct	tgg	gaa	gtg	tac	ggc	agg	aac	gac	tct	cgt	ctc	acg	1107
Tyr	Gln	Ile	Ser	Trp	Glu	Val	Tyr	Gly 236/		Asn	Asp	Ser	Arg	Leu	Thr	

	350			355					360			
cac acc ctg	_											1155
365			3	70				375				
tct ctc acc	acc tac	acc a	atc g	ac gtg	gcc	gct	gtg	act	gcc	gtg	ggc	1203
Ser Leu Thr	Thr Tyr	Thr 1	Ile A	sp Val	Ala	Ala	Val	Thr	Ala	Val	Gly	
380		3	385				390					
act ggc ctg	gtg act	tca t	tcc a	cc att	tct	tct	gga	gtg	ccc	cca	gac	1251
Thr Gly Leu	Val Thr	Ser S	Ser T	hr Ile	Ser	Ser	Gly	Val	Pro	Pro	Asp	
395		400				405					410	
ctt cct ggt												1299
Leu Pro Gly		Ser A	Asn L	eu Val	Ile	Ser	Asn	Ile	Ser	Pro	Arg	
	415				420					425		
												1047
tcc gcc acc								_		_		1347
Ser Ala Thr		Pne A	Arg P		lyr	Asp	GIA	Lys		Ser	116	
	430			435					440		•	
+00 000 +00	o++ #++	go g _ /	a	oa ota	0.00	oo+	000	aat	at t	~~	++0	1205
tcc agg tgg												1395
Ser Arg Trp	ite var	Giu (Arg	пта	GIII		Val	Gly	Leu	
445			4	50				455				
cct gcc gag	gtc aca	cag	сса я	go cat	gaa	gcc	gga	ttg	gag	cct	gca	1443

465

460

470

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aac ctc gga agt ctg tgg ctg ctc agc ctg gtg tat tgg tgt tac agc 1491
Asn Leu Gly Ser Leu Trp Leu Leu Ser Leu Val Tyr Trp Cys Tyr Ser
475 480 485 490

cag aaa ctt tgg gaa ttc tct tgt tagttggtta gttttactgt aattttctat 1545 Gln Lys Leu Trp Glu Phe Ser Cys

495

aaagaattca tatcatctgt taatggcgac agtttttgtt tetteetttg aatttttat 1605
attettett tetettttt gtttettett etttgagtat tttgtaatet taetgggagg 1665
getaaagegt ettetateat ategaattgg gacaatgata gaagacaate tttgttttgt 1725
caetetaaag aaattattgt aagatttat eateaggtat gacatttaca eeattgatgt 1785
aggetttta aaaaatatat eeageetgta ttgggttaag atgattett tetgateetg 1845
attteetagg agttggtttt tttttttta aageataaat aaatttaatt geateag 1902

<210> 71

<211> 245

<212> PRT

<213> Homo sapiens

<400> 71

Met Pro Val Gln Leu Ser Glu His Pro Glu Trp Asn Glu Ser Met His 238/735

W	O 02/	05373	7												PCT/JP01/11389
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Ser	Leu	Arg		Ser	Val	Gly	Gly		Pro	Val	Leu	Ala		Met	Thr
			20					25					30		
Lys	Ala	Ala	Asp	Pro	Arg	Phe	Arg	Pro	Arg	Trp	Lys	Val	Ile	Leu	Thr
		35					40					45			
								_							_
Phe	Phe 50	Val	Gly	Ala	Ala	Ile 55	Leu	Trp	Leu	Leu	Cys 60	Ser	His	Arg	Pro
	00					00					00				
Ala	Pro	G1y	Arg	Pro	Pro	Thr	His	Asn	Ala	His	Asn	Trp	Arg	Leu	Gly
65					70					75					80
C1-	A1 a	Dma	41a	Aan	Т	Т	A an	A ===	Ть	Turn	Dwo	Lou	Sor	Dwo	Pro
GIII	Ala	FIO	нта	85	11р	1 91	ASII	KSP	90	I yI.	Pro	Leu	Set	95	110
G1n	Arg	Thr	Pro	Ala	Gly	Ile	Arg	Tyr	Arg	Ile	Ala	Val	Ile	Ala	Asp
			100					105					110		
Leu	Asp	Thr	Glu	Ser	Arg	Ala	Gln	Glu	Glu	Asn	Thr	Trp	Phe	Ser	Tyr
	•	115		•	J	-	120					125			-
Leu	Lys	Lys	Gly	Tyr	Leu	Thr	Leu	Ser	Asp	Ser	Gly	Asp	Lys	Val	Ala

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Val Glu Trp Asp Lys Asp His Gly Val Leu Glu Ser His Leu Ala Glu

Lys Gly Arg Gly Met Glu Leu Ser Asp Leu Ile Val Phe Asn Gly Lys
165 170 175

Leu Tyr Ser Val Asp Asp Arg Thr Gly Val Val Tyr Gln Ile Glu Gly
180 185 190

Ser Lys Ala Val Pro Trp Val Ile Leu Ser Asp Gly Asp Gly Thr Val 195 200 205

Glu Lys Gly Phe Lys Ala Glu Trp Leu Ala Val Arg Glu Ile Val Arg 210 215 220

Lys Arg Trp Arg Leu Val Lys Gln Val Ser His Val Gly Val Leu Gly
225 230 235 240

Gln Trp Ile Gln Arg

245

<210> 72

<211> 1551

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (127).. (861)

<400> 72

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ccaa	agcc	ccg	ccga	tcgc	gg g	cacc	ggago	c ca	gccc	cgca	gcg	ggtc	ccg	cctg	tctgtc	120
acgo			ccc													168
			Pro	Val	Gln .		Ser (Glu	His	Pro (Trp .	Asn	Glu S	Ser	
		1				5					10					
atg	cad	tco	ctc	cgg	atc	agt	gtg	ggg	ggc	ctt	cct	gtg	ctg	gcg	tcc	216
			Leu													
15				0	20					25					30	
atg	acc	aag	gcc	gcg	gac	ccc	cgc	ttc	cgc	ccc	cgc	tgg	aag	gtg	atc	264
Met	Thr	Lys	Ala	Ala	Asp	Pro	Arg	Phe	Arg	Pro	Arg	Trp	Lys	Val	Ile	
				35					40					45		
ctg	acg	tto	ttt	gtg	ggt	gct	gcc	atc	ctc	tgg	ctg	ctc	tgc	tcc	cac	312
Leu	Thr	Phe	Phe	Val	Gly	Ala	Ala	Ile	Leu	Trp	Leu	Leu	Cys	Ser	His	
			50					55					60			
cgc	ccg	gcc	ccc	ggc	agg	ccc	ccc	acc	cac	aat	gca	cac	aac	tgg	agg	360
Arg	Pro	Ala	Pro	G1y	Arg	Pro	Pro	Thr	His	Asn	Ala	His	Asn	Trp	Arg	
		65	j				70					75				
												.				400
	_		gcg													408
Leu			Ala	Pro	ATS		irp	ıyr	ASII	Asp	90	1 9 Γ	Pro	Leu	ser	
	80	,				85					30					
ccc	cca	caa	agg	aca	ccg	gct	ggg		cgg /735	tat	cga	atc	gca	gtt	atc	456

Pro	Pro	Gln	Arg	Thr	Pro	Ala	Gly	Ile	Arg	Tyr	Arg	Ile	Ala	Val	Ile	
95					100					105					110	
gca	gac	ctg	gac	aca	gag	tca	agg	gcc	caa	gag	gaa	aac	acc	tgg	ttc	504
Ala	Asp	Leu	Asp	Thr	G1u	Ser	Arg	Ala	Gln	Glu	Glu	Asn	Thr	Trp	Phe	
				115					120					125		
agt	tac	ctg	aaa	aag	ggc	tac	ctg	acc	ctg	tca	gac	agt	ggg	gac	aag	552
Ser	Tyr	Leu	Lys	Lys	Gly	Tyr	Leu	Thr	Leu	Ser	Asp	Ser	Gly	Asp	Lys	
			130					135					140			
gtg	gcc	gtg	gaa	tgg	gac	aaa	gac	cat	ggg	gtc	ctg	gag	tcc	cac	ctg	600
Val	Ala	Val	Glu	Trp	Asp	Lys	Asp	His	Gly	Val	Leu	Glu	Ser	His	Leu	
		145					150					155				
gcg	gag	aag	ggg	aga	ggc	atg	gag	cta	tcc	gac	ctg	att	gtt	ttc	aat	648
Ala	Glu	Lys	Gly	Arg	G1y	Met	Glu	Leu	Ser	Asp	Leu	Ile	Val	Phe	Asn	
	160					165					170					
ggg	aaa	ctc	tac	tcc	gtg	gat	gac	cgg	acg	ggg	gtc	gtc	tac	cag	atc	696
Gly	Lys	Leu	Tyr	Ser	Val	Asp	Asp	Arg	Thr	Gly	Val	Val	Tyr	Gln	Ile	
175					180					185					190	
gaa	ggc	agc	aaa	gcc	gtg	ссс	tgg	gtg	att	ctg	tcc	gac	ggc	gac	ggc	744
Glu	Gly	Ser	Lys	Ala	Val	Pro	Trp	Val	Ile	Leu	Ser	Asp	Gly	Asp	Gly	
				195					200					205		
acc	gtg	gag	aaa	ggc	ttc	aag	gcc	gaa	tgg	ctg	gca	gtg	cgg	gag	att	792
Γhr	Val	Glu	Lys	G1y	Phe	Lys	Ala	Glu	Trp	Leu	Ala	Val	Arg	Glu	Ile	
								242/	735							

210 215 220

gta agg aag cgg tgg cgg ctg gtg aag caa gtc tca cat gtc ggc gtt 840
Val Arg Lys Arg Trp Arg Leu Val Lys Gln Val Ser His Val Gly Val
225 230 235

ctt ggc caa tgg ata caa aga taaagaaaat gttgcctttt tctaggaact 891 Leu Gly Gln Trp Ile Gln Arg 240 245

gtcagaaatc ctcatgcctt tcaagacttc tgtgaatgac ttgaatttt tattccctgc 951
ctagggtctg tgaacgaggc ctgtctcttc cctggggttt ctttccatgg cctttatttc 1011
tcctcttcca gtgggagttt tgcaggctct tctctgtgga aacttcacga gcgttggctg 1071
ggcctcggct tcgctggagt gtactccagg gtgaaggcag agtgggattt gagacccagg 1131
tagtggagga agcgaaggaa gtgaacgctg aatgtgacgc atttctgaag agctcagctg 1191
tcaccgggca tagcctggaa gccccaagtc tgttctgact ttgcctggct gtctccttga 1251
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gcgattactt taaagctcac cttttttctt cccctctctg ttcgctgct tcagcataat 1491
243/735

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<210> 73

<211> 352

<212> PRT

<213> Homo sapiens

<400> 73

Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly

1 5 10 15

Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys
20 25 30

Ala Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val His Leu Gly
35 40 45

Glu Asp Leu Lys Ser Ile Leu Ser Glu Ala Pro Gly Lys Cys Val Pro
50 55 60

Tyr Ala Val Ile Glu Gly Ala Val Arg Ser Val Lys Glu Thr Leu Asn 65 70 75 80

Ser Gln Phe Val Glu Asn Cys Lys Gly Val Ile Gln Arg Leu Thr Leu 85 90 95

Gln Glu His Lys Met Val Trp Asn Arg Thr Thr His Leu Trp Asn Asp 244/735

V	VO 02	/0537:	37												PCT/JP01/11389
			100					105					110		
Cys	Ser	Lys 115	Ile	Ile	His	Gln	Arg 120	Thr	Asn	Thr	Val	Pro 125	Phe	Asp	Leu
Val	Pro 130	His	Glu	Asp	Gly	Val 135	Asp	Val	Ala	Val	Arg 140	Val	Leu	Lys	Pro
Leu 145	Asp	Ser	Val	Asp	Leu 150	Gly	Leu	G1u	Thr	Val 155	Tyr	G1u	Lys	Phe	His 160
Pro	Ser	Ile	Gln	Ser 165	Phe	Thr	Asp	Val	Ile 170	Gly	His	Tyr	Ile	Ser 175	Gly

Glu Arg Pro Lys Gly Ile Gln Glu Thr Glu Glu Met Leu Lys Val Gly
180 185 190

Ala Thr Leu Thr Gly Val Gly Glu Leu Val Leu Asp Asn Asn Ser Val
195 200 205

Arg Leu Gln Pro Pro Lys Gln Gly Met Gln Tyr Tyr Leu Ser Ser Gln
210 215 220

Asp Phe Asp Ser Leu Leu Gln Arg Gln Glu Ser Ser Val Arg Leu Trp 225 230 235 240

Lys Val Leu Ala Leu Val Phe Gly Phe Ala Thr Cys Ala Thr Leu Phe
245 250 255

Phe Ile Leu Arg Lys Gln Tyr Leu Gln Arg Gln Glu Arg Leu Arg Leu 260 265 270

Lys Gln Met Gln Glu Glu Phe Gln Glu His Glu Ala Gln Leu Leu Ser 275 280 285

Arg Ala Lys Pro Glu Asp Arg Glu Ser Leu Lys Ser Ala Cys Val Val 290 295 300

Cys Leu Ser Ser Phe Lys Ser Cys Val Phe Leu Glu Cys Gly His Val 305 310 315 320

Cys Ser Cys Thr Glu Cys Tyr Arg Ala Leu Pro Glu Pro Lys Lys Cys 325 330 335

Pro Ile Cys Arg Gln Ala Ile Thr Arg Val Ile Pro Pro Tyr Asn Ser 340 345 350

<210> 74

<211> 2401

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (103).. (1158)

<400> 74

PCT/JP01/11389
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tato	cctt	ggc (gcca	cagto	og go	ccac	eggg	g ct	cgcc	gccg				agc (114
ggg	cgg	ccc	tcg	ctg.	tgc	cag	ttc	atc	ctc	ctg	ggc	acc	acc	tct	gtg	162
G1y	Arg	Pro	Ser	Leu	Cys	G1n	Phe	Ile	Leu	Leu	Gly	Thr	Thr	Ser	Val	
5					10					15					20	
gtc	acc	gcc	gcc	ctg	tac	tcc	gtg	tac	cgg	cag	aag	gcc	cgg	gtc	tcc	210
Val	Thr	Ala	Ala	Leu	Tyr	Ser	Val	Tyr	Arg	Gln	Lys	Ala	Arg	Val	Ser	
				25					30					35		
caa	gag	ctc	aag	gga	gct	aaa	aaa	gtt	cat	ttg	ggt	gaa	gat	tta	aag	258
Gln	Glu	Leu	Lys	G1y	Ala	Lys	Lys	Val	His	Leu	Gly	Glu	Asp	Leu	Lys	
			40					45					50			
agt	att	ctt	tca	gaa	gct	cca	gga	aaa	tgc	gtg	cct	tat	gct	gtt	ata	306
Ser	Ile	Leu	Ser	Glu	Ala	Pro	Gly	Lys	Cys	Val	Pro	Tyr	Ala	Val	Ile	
		55					60					65				
gaa	gga	gct	gtg	cgġ	tct	gtt	aaa	gaa	acg	ctt	aac	agc	cag	ttt	gtg	354
Glu	Gly	Ala	Val	Arg	Ser	Val	Lys	Glu	Thr	Leu	Asn	Ser	Gln	Phe	Val	
	70					75					80					
gaa	aac	tgc	aag	ggg	gta	att	cag	cgg	ctg	aca	ctt	cag	gag	cac	aag	402
Glu	Asn	Cys	Lys	Gly	Val	Ile	Gln	Arg	Leu	Thr	Leu	Gln	Glu	His	Lys	
85					90			•		95					100	
								247	/735							

atg	gtg	tgg	aat	cga	acc	acc	cac	ctt	tgg	aat	gat	tgc	tca	aag	atc	450
Met	Val	Trp	Asn	Arg	Thr	Thr	His	Leu	Trp	Asn	Asp	Cys	Ser.	Lys	Ile	
				105					110					115		
att	cat	cag	agg	acc	aac	aca	gtg	ссс	ttt	gac	ctg	gtg	ccc	cac	gag	498
Ile	His	Gln	Arg	Thr	Asn	Thr	Val	Pro	Phe	Asp	Leu	Val	Pro	His	Glu	
			120					125					130			
gat	ggc	gtg	gat	gtg	gct	gtg	cga	gtg	ctg	aag	ccc	ctg	gac	tca	gtg	546
Asp	G1y	Val	Asp	Val	Ala	Val	Arg	Val	Leu	Lys	Pro	Leu	Asp	Ser	Val	
		135					140					145				
gat	ctg	ggt	cta	gag	act	gtg	tat	gag	aag	ttc	cac	ccc	tcg	att	cag	594
Asp	Leu	Gly	Leu	Glu	Thr	Val	Tyr	Glu	Lys	Phe	His	Pro	Ser	Ile	Gln	
	150					155					160	•				
											ggt					642
	Phe	Thr	Asp	Val		Gly	His	Tyr	lle		Gly	Glu	Arg	Pro		
165					170					175					180	
																200
										_	ggg					690
GIA	116	GIN	Giu		Glu	GLU	Met	Leu		vaı	Gly	Ala	Inr		inr	
				185					190					195		
										4.4						720
	-										gtc				_	738
στλ	vaı	GIÀ		ren	val	Leu	Asp		ASN	ser	Val	Arg		GIU	rro	
			200					205					210			

ccc	aaa	caa	ggc	atg	cag	tac	tat	cta	agc	agc	cag	gac	ttc	gac	agc	786
Pro	Lys	Gln	Gly	Met	Gln	Tyr	Tyr	Leu	Ser	Ser	Gln	Asp	Phe	Asp	Ser	
		215					220					225				
ctg	ctg	cag	agg	cag	gag	tcg	agc	gtc	agg	ctc	tgg	aag	gtg	ctg	gcg	834
Leu	Leu	G1n	Arg	G1n	Glu	Ser	Ser	Val	Arg	Leu	Trp	Lys	Val	Leu	Ala	
	230					235					240					
												•				
ctg	gtt	ttt	ggc	ttt	gcc	aca	tgt	gcc	acc	ctc	ttc	ttc	att	ctc	cgg	882
Leu	Val	Phe	Gly	Phe	Ala	Thr	Cys	Ala	Thr	Leu	Phe	Phe	Ile	Leu	Arg	
245					250					255					260	
aag	cag	tat	ctg	cag	cgg	cag	gag	cgc	ctg	cgc	ctc	aag	cag	atg	cag	930
Lys	Gln	Tyr	Leu	Gln	Arg	G1n	G1u	Arg	Leu	Arg	Leu	Lys	Gln	Met	G1n	
				265					270					275		
gag	gag	ttc	cag	gag	cat	gag	gcc	cag	ctg	ctg	agc	cga	gcc	aag	cct	978
Glu	Glu	Phe	Gln	Glu	His	Glu	Ala	Gln	Leu	Leu	Ser	Arg	Ala	Lys	Pro	•
			280					285					290			
gag	gac	agg	gag	agt	ctg	aag	agc	gcc	tgt	gta	gtg	tgt	ctg	agc	agc	1026
Glu	Asp	Arg	G1u	Ser	Leu	Lys	Ser	Ala	Cys	Val	Val	Cys	Leu	Ser	Ser	
		295					300					305				
ttc	aag	tcc	tgc	gtc	ttt	ctg	gag	tgt	ggg	cac	gtt	tgt	tcc	tgc	acc	1074
Phe	Lys	Ser	Cys	Val	Phe	Leu	Glu	Cys	Gly	His	Val	Cys	Ser	Cys	Thr	
	310					315					320				,	
gag	tgc	tac	cgc	gcc	ttg	cca	gag	ссс	aag	aag	tgc	cct	atc	tgc	aga	1122
							•	249/	735							

Glu Cys Tyr Arg Ala Leu Pro Glu Pro Lys Lys Cys Pro Ile Cys Arg 325 330 335 340

cag gcg atc acc cgg gtg ata ccc ccg tac aac agc taatagtttg 1168

Gln Ala Ile Thr Arg Val Ile Pro Pro Tyr Asn Ser

345 350

gaagccgcac agcttgacct ggaagcaccc ctgccccctt ttcagggatt tttatctcga 1228 ggcctttgga ggagcagtgg tgggggtagc tgtcacctcc aggtatgatt gagggaggaa 1288 tegggtagaa actetecaga eccatgeete caatggeagg atgetgeett teecacetga 1348 gaggggaccc tgtccatgtg cagcctcatc agagcctcac cctgggagga tgccgtggcg 1408 tetectecca ggagecagat cagtgegagt gtgactgaaa atgeeteate aettaageae 1468 caaagccagt gatcagcagc tettetgtte etgtgtette tgttttttte tggtgaateg 1528 ttgcttgctg tggacttggt ggaggactca gaggggagga aaggctgggc cccgagtaca 1588 acggatgcct tgggtgctgc ctccgaagag actctgccgc agcttttctt ctttttcctc 1648 atgccccggg aaacagtctt tcttcagaat tgtcaggctg ggcaggtcaa cttgtgttcc 1708 tttcccctca cctgcttgcc tccttaacgc ctgcacgtgt gtgtagagga caaaagaaag 1768 tgaagtcagc acatccgctt ctgcccagat ggtcggggcc ccgggcaaca gattgaagag 1828

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gagcctttta gtgcaagaca gatggggctg ttttcccca cctctgagta gttggaggtc 2248
acatacacag ctctttttt attgcccttt tctgcctctg aatgttcatc tctcgtcctc 2308
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gtgtgaacag cagaaattaa acatgttgca acc 2401

<210> 75

<211> 352

<212> PRT

<213> Homo sapiens

<400> 75

Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly

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Thr	Thr	Ser	Val 20	Val	Thr	Ala	Ala	Leu 25	Tyr	Ser	Val	Tyr	Arg 30	Gln	Lys
Ala	Arg		Ser	Gln	Glu	Leu		Gly	Ala	Lys	Lys	Val	His	Leu	Gly
		35					40					45			
G1u	Asp	Leu	Lys	Ser	Ile	Leu	Ser	G1u	Ala	Pro	G1y	Lys	Cys	Val	Pro
	50					55					60				
Tyr	Ala	Val	Ile	Glu	Gly	Ala	Val	Arg	Ser	Va1	Lys	Glu	Thr	Leu	Asn
65					70					75					80
Som	Gln.	Dho	Vo 1	Cl.,	Aan	Cva	Lvo	C1	Vol.	T1.	C1-	A	T	TL	T
pet	GIII	rne	Val	85	ASII	Cys	Lys	GIY	90	TTE	GIII	Arg	Leu	95	Leu
				00					50					50	
G1n	G1u	His	Lys	Met	Val	Trp	Asn	Arg	Thr	Thr	His	Leu	Trp	Asn	Asp
			100					105					110		
Cve	Sor	Ive	Τlο	בוז	Hic	Gln.	Ara	Thr	Acn	Thr	Vol.	Dro	Dha	Aon	Lou
Cys	Der	115	116	116	1112	GIII	120	1111	VSII	1111	Val	Pro 125	rne	ASP	Leu
		110					120					120			
Val	Pro	His	Glu	Asp	Gly	Val	Asp	Val	Ala	Val	Arg	Val	Leu	Lys	Pro
	130					135					140				
נום ז	Aen	Sor	Va1	Asn	Low	C1 12	Lou	G1,,	Thr	Val	Turn	Glu	I wa	Dhe	u:c
145	ush	SeT	۷ a 1	vsh		о т у	Leu	JIU	1111		Tyr	GIU	LyS	LIIG	
140					150					155					160

Pro Ser Ile Gl
n Ser Phe Thr Asp Val Ile Gly His Tyr Ile Ser Gly $\,$

W	O 02	(0537	37												PCT/JP01/11389
				165					170					175	
Glu	Arg	Pro	Lys 180	Gly	Ile	G1n	Glu	Thr 185	G1u	Glu	Met	Leu	Lys 190	Val	Gly
Ala	Thr	Leu 195	Thr	Gly	Val	G1y	Glu 200	Leu	Val	Leu	Asp	Asn 205	Asn	Ser	Val
Arg	Leu 210	G1n	Pro	Pro	Lys	G1n 215	Gly	Met	Gln	Tyr	Tyr 220	Leu	Ser	Ser	Gln
Asp 225	Phe	Asp	Ser	Leu	Leu 230	Gln	Arg	Gln	Glu	Ser 235	Ser	Val	Arg	Leu	Trp 240
Lys	Val	Leu	Ala	Leu 245	Val	Phe	Gly	Phe	Ala 250	Thr	Cys	Ala	Thr	Leu 255	Phe
Phe	Ile	Leu	Arg 260	Lys	Gln	Tyr	Leu	Gln 265	Arg	Gln	Glu	Arg	Leu 270	Arg	Leu
Lys	Gln	Met 275	Gln	Glu	G1u	Phe	G1n 280	Glu	His	G1u	Ala	G1n 285	Leu	Leu	Ser
Arg	Ala 290	Lys	Pro	G1u	Asp	Arg 295	G1u	Ser	Leu	Lys	Ser 300	Ala	Cys	Val	Val

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Cys Leu Ser Ser Phe Lys Ser Cys Val Phe Leu Glu Cys Gly His Val

Cys Ser Cys Thr Glu Cys Tyr Arg Ala Leu Pro Glu Pro Lys Lys Cys 325 330 335

Pro Ile Cys Arg Gln Ala Ile Thr Arg Val Ile Pro Leu Tyr Asn Ser 340 345 350

<210> 76

<211> 2401

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (103).. (1158)

<400> 76

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Met Glu Ser Gly

1

ggg cgg ccc tcg ctg tgc cag ttc atc ctc ctg ggc acc acc tct gtg 162
Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly Thr Thr Ser Val
5 10 15 20

gtc acc gcc gcc ctg tac tcc gtg tac cgg cag aag gcc cgg gtc tcc 210
Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys Ala Arg Val Ser
254/735

				25					30					35		
caa	gag	ctc	aag	gga	gct	aaa	aaa	gtt	cat	ttg	ggt	gaa	gat	tta	aag	258
Gln	Glu	Leu	Lys	Gly	Ala	Lys	Lys	Val	His	Leu	Gly	Glu	Asp	Leu	Lys	
			40					45					50			
													-			
agt	att	ctt	tca	gaa	gct	cca	gga	aaa	tgc	gtg	cct	tat	gct	gtt	ata	306
Ser	Ile	Leu	Ser	G1u	Ala	Pro	Gly	Lys	Cys	Val	Pro	Tyr	Ala	Val	Ile	
		55					60					65				•
gaa	gga	gct	gtg	cgg	tct	gtt	aaa	gaa	acg	ctt	aac	agc	cag	ttt	gtg	354
G1u	Gly	Ala	Val	Arg	Ser	Val	Lys	Glu	Thr	Leu	Asn	Ser	Gln	Phe	Val	
	70					75					80	-				
gaa	aac	tgc	aag	ggg	gta	att	cag	cgg	ctg	aca	ctt	cag	gag	cac	aag	402
Glu	Asn	Cys	Lys	Gly	Val	Ile	Gln	Arg	Leu	Thr	Leu	Gln	Glu	His	Lys	
85					90					95					100	
														aag		450
Met	Val	Trp	Asn		Thr	Thr	His	Leu		Asn	Asp	Cys	Ser	Lys	Ile	
				105					110					115		
											4					400
														cac		498
116	піѕ	GIN		Inr	ASII	1111	val		rne	ASP	reu	Val		His	GIU	
			120					125					130			
gat	gge	gt o	gat	øtø	get	gt.o	Cga	ot o	cta	ឧឧក	ccc	ctø	gac	tca	gte	546
									_					Ser		0.20
	,		p				5	, ur	1,011	ت و ب						

140

255/735

145

PCT/JP01/11389

WO 02/053737

135

gat	ctg	ggt	cta	gag	act	gtg	tat	gag	aag	ttc	cac	ccc	tcg	att	cag	594
Asp	Leu	Gly	Leu	Glu	Thr	Val	Tyr	Glu	Lys	Phe	His	Pro	Ser	Ile	Gln	
	150					155					160					
tcc	ttc	acc	gat	gtc	atc	ggc	cac	tac	atc	agc	ggt	gag	cgg	ссс	aaa	642
Ser	Phe	Thr	Asp	Val	Ile	G1y	His	Tyr	Ile	Ser	Gly	Glu	Arg	Pro	Lys	
165					170					175					180	
ggc	atc	caa	gag	acc	gag	gag	atg	ctg	aag	gtg	ggg	gcc	acc	ctc	aca	690
Gly	Ile	Gln	Glu	Thr	Glu	Glu	Met	Leu	Lys	Val	Gly	Ala	Thr	Leu	Thr	
				185					190					195		
ggg	gtt	ggc	gaa	ctg	gtc	ctg	gac	aac	aac	tct	gtc	cgc	ctg	cag	ccg	738
G1y	Val	Gly	Glu	Leu	Val	Leu	Asp	Asn	Asn	Ser	Val	Arg	Leu	Gln	Pro	
			200					205					210			
ссс	aaa	caa	ggc	atg	cag	tac	tat	cta	agc	agc	cag	gac	ttc	gac	agc	786
Pro	Lys	Gln	Gly	Met	G1n	Tyr	Tyr	Leu	Ser	Ser	Gln	Asp	Phe	Asp	Ser	
		215					220					225				
ctg	ctg	cag	agg	cag	gag	tcg	agc	gtc	agg	ctc	tgg	aag	gtg	ctg	gcg	834
Leu	Leu	Gln	Arg	G1n	Glu	Ser	Ser	Val	Arg	Leu	Trp	Lys	Val	Leu	Ala	
	230					235					240					
ctg	gtt	ttt	ggc	ttt	gcc	aca	tgt	gcc	acc	ctc	ttc	ttc	att	ctc	cgg	882
Leu	Val	Phe	Gly	Phe	Ala	Thr	Cys	Ala	Thr	Leu	Phe	Phe	Ile	Leu	Arg	
245					250					255					260	

aag	cag	tat	ctg	cag	cgg	cag	gag	cgc	ctg	cgc	ctc	aag	cag	atg	cag	930
Lys	Gln	Tyr	Leu	Gln	Arg	Gln	Glu	Arg	Leu	Arg	Leu	Lys	Gln	Met	Gln	
				265					270					275		
gag	gag	ttc	cag	gag	cat	gag	gcc	cag	ctg	ctg	agc	cga	gcc	aag	cct	978
Glu	Glu	Phe	Gln	Glu	His	Glu	Ala	Gln	Leu	Leu	Ser	Arg	Ala	Lys	Pro	
			280					285			-		290			
gag	gac	agg	gag	agt	ctg	aag	agc	gcc	tgt	gta	gtg	tgt	ctg	agc	agc	1026
Glu	Asp	Arg	Glu	Ser	Leu	Lys	Ser	Ala	Cys	Val	Val	Cys	Leu	Ser	Ser	
		295					300					305				
ttc	aag	tcc	tgc	gtc	ttt	ctg	gag	tgt	ggg	cac	gtt	tgt	tcc	tgc	acc	1074
Phe	Lys	Ser	Cys	Val	Phe	Leu	Glu	Cys	Gly	His	Val	Cys	Ser	Cys	Thr	
	310					315					320					
gag	tgc	tac	cgc	gcc	ttg	cca	gag	ccc	aag	aag	tgc	cct	atc	tgc	aga	1122
Glu	Cys	Tyr	Arg	Ala	Leu	Pro	Glu	Pro	Lys		Cys	Pro	Ile	Cys	Arg	
325					330					335					340	
				cgg								taat	agti	ttg		1168
Gln	Ala	He	Thr	Arg	Val	lle	Pro	Leu		Asn	Ser					
				345					350							
											++					1000
gaag	ccgc	cac a	igcti	gaco	t gg	gaago	acco	CTE	geeec	CLL	LLCE	ıggga	וננ ו	tttai	ctcga	1228
~~~				+ .	·~ +.		***	. +~+		+00	aggt	. a t a a	.++ .	~~~~		1200
RRCC	: L L T &	gga g	gago	agug	sg r	RRRE	stago	; cgt	,cacc	, 600	aggl	auga	<b>{</b>	sagge	gaggaa	1200
+0~-	rat o o	*OC -	+4	-000	Ta 01	.os+-	root -		+ ~ ~	aaa	atos	+ 000	·++ +	taaa	natas	12/0
rogg	Rraf	saa 8	10 i CT	LUUME	sa cc	ocale	50010	257/		agg	augl	, rgc(	,66	LUUUE	icctga	1040

gaggggaccc tgtccatgtg cagcctcatc agagcctcac cctgggagga tgccgtggcg 1408 tetectecca ggagecagat cagtgegagt gtgactgaaa atgeeteate aettaageae 1468 caaagccagt gatcagcagc tettetgtte etgtgtette tgttttttte tggtgaateg 1528 ttgcttgctg tggacttggt ggaggactca gaggggagga aaggctgggc cccgagtaca 1588 acggatgcct tgggtgctgc ctccgaagag actctgccgc agcttttctt ctttttcctc 1648 atgccccggg aaacagtctt tcttcagaat tgtcaggctg ggcaggtcaa cttgtgttcc 1708 tttcccctca cctgcttgcc tccttaacgc ctgcacgtgt gtgtagagga caaaagaaag 1768 tgaagtcagc acatccgctt ctgcccagat ggtcggggcc ccgggcaaca gattgaagag 1828 agateatgtg aagggeagtt ggteaggeag geeteetggt ttegeeactg geeetgattt 1888 gaactcctgc cacttgggag agctcggggt ggtccctggt tttccctcct ggagaatgag 1948 gegeagagge ctegeeteet gaaggaegea gtgtggatge caetggeeta gtgteetgge 2008 ctcacagctt ccttgcaagg ctgtcacaag gaaaagcagc cggctggcac cctgagcata 2068 tgccctcttg gggctccctc atccagcccg tcgcagcttt gacatcttgg tgtactcatg 2128 tegettetee ttgtgttace ceeteceagt attaceattt geeceteace tgeecttggt 2188

gagcctttta gtgcaagaca gatggggctg ttttccccca cctctgagta gttggaggtc 2248
acatacacag ctctttttt attgcccttt tctgcctctg aatgttcatc tctcgtcctc 2308
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gtgtgaacag cagaaattaa acatgttgca acc 2401

<210> 77

<211> 697

<212> PRT

<213> Homo sapiens

<400> 77

Met Cys Lys Ser Leu Arg Tyr Cys Phe Ser His Cys Leu Tyr Leu Ala

1 5 10 15

Met Thr Arg Leu Glu Glu Val Asn Arg Glu Val Asn Met His Ser Ser
20 25 30

Val Arg Tyr Leu Gly Tyr Leu Ala Arg Ile Asn Leu Leu Val Ala Ile 35 40 45

Cys Leu Gly Leu Tyr Val Arg Trp Glu Lys Thr Ala Asn Ser Leu Ile 50 55 60

Leu Val Ile Phe Ile Leu Gly Leu Phe Val Leu Gly Ile Ala Ser Ile
65 70 75 80
259/735

Leu	Tyr	Tyr	Tyr	Phe 85	Ser	Met	Glu	Ala	Ala 90	Ser	Leu	Ser	Leu	Ser 95	Asn
Leu	Trp	Phe	Gly 100	Phe	Leu	Leu	Gly	Leu 105	Leu	Cys	Phe	Leu	Asp 110	Asn	Ser
Ser	Phe	Lys 115	Asn	Asp	Val	Lys	Glu 120	Glu	Ser	Thr	Lys	Tyr 125	Leu	Leu	Leu
Thr	Ser 130	Ile	Val	Leu	Arg	Ile 135	Leu	Cys	Ser	Leu	Val 140	Glu	Arg	Ile	Ser
Gly 1 <b>4</b> 5	Tyr	Val	Arg	His	Arg 150	Pro	Thr	Leu	Leu	Thr 155	Thr	Val	Glu	Phe	Leu 160
G1u	Leu	Val	Gly	Phe 165	Ala	Ile	Ala	Ser	Thr 170	Thr	Met	Leu	Val	G1u 175	Lys
Ser	Leu	Ser	Val 180	Ile	Leu	Leu	Val	Val 185	Ala	Leu	Ala	Met	Leu 190	Ile	Ile
Asp	Leu	Arg 195	Met	Lys	Ser	Phe	Leu 200	Ala	Ile	Pro	Asn	Leu 205	Val	Ile	Phe
Ala	Val 210	Leu	Leu	Phe	Phe	Ser 215	Ser	Leu	Glu	Thr	Pro 220	Lys	Asn	Pro	Ile
Ala	Phe	Ala	Cvs	Phe	Phe	Tle	Cvs	Len	۲۱۵	Thr	Asn	Pro	Phe	Len	Aen.

225					230					235					240
Ile	Tyr	Phe	Ser	Gly 245	Leu	Ser	Val	Thr	G1u 250	Arg	Trp	Lys	Pro	Phe 255	Leu
Tyr	Arg	Gly	Arg 260	Ile	Cys	Arg	Arg	Leu 265	Ser	Val	Val	Phe	Ala 270	Gly	Met
Ile	Glu	Leu 275	Thr	Phe	Phe	Ile	Leu 280	Ser	Ala	Phe	Lys	Leu 285	Arg	Asp	Thr
His	Leu 290	Trp	Tyr	Phe	Val	Ile 295	Pro	Gly	Phe	Ser	Ile 300	Phe	Gly	Ile	Phe
Trp 305	Met	Ile	Cys	His	Ile 310	Ile	Phe	Leu	Leu	Thr 315	Leu	Trp	Gly	Phe	His
Thr	Lys	Leu	Asn	Asp 325	Cys	His	Lys	Val	Tyr 330	Phe	Thr	His	Arg	Thr 335	Asp
Tyr	Asn	Ser	Leu 340	Asp	Arg	Ile	Met	Ala 345	Ser	Lys	G1y	Met	Arg 350	His	Phe
Cys	Leu	Ile 355	Ser	Glu	Gln	Leu	Val 360	Phe	Phe	Ser	Leu	Leu 365	Ala	Thr	Ala
Ile	Leu 370	Gly	Ala	Val	Ser	Trp 375	Gln	Pro	Thr	Asn	Gly 380	Ile	Phe	Leu	Ser

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XO 02/053737	PCT/JP01/11389

Met	Phe	Leu	Ile	Val	Leu	Pro	Leu	Glu	Ser	Met	Ala	His	Gly	Leu	Phe
385					390					395					400

His Glu Leu Gly Asn Cys Leu Gly Gly Thr Ser Val Gly Tyr Ala Ile
405 410 415

Val Ile Pro Thr Asn Phe Cys Ser Pro Asp Gly Gln Pro Thr Leu Leu
420 425 430

Pro Pro Glu His Val Gln Glu Leu Asn Leu Arg Ser Thr Gly Met Leu
435 440 445

Asn Ala Ile Gln Arg Phe Phe Ala Tyr His Met Ile Glu Thr Tyr Gly
450 455 460

Cys Asp Tyr Ser Thr Ser Gly Leu Ser Phe Asp Thr Leu His Ser Lys
465 470 475 480

Leu Lys Ala Phe Leu Glu Leu Arg Thr Val Asp Gly Pro Arg His Asp
485 490 495

Thr Tyr Ile Leu Tyr Tyr Ser Gly His Thr His Gly Thr Gly Glu Trp
500 505 510

Ala Leu Ala Gly Gly Asp Thr Leu Arg Leu Asp Thr Leu Ile Glu Trp
515 520 525

Trp Arg Glu Lys Asn Gly Ser Phe Cys Ser Arg Leu Ile Ile Val Leu
530 535 540
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Asp Ser Glu Asn Ser Thr Pro Trp Val Lys Glu Val Arg Lys Ile Asn Asp Gln Tyr Ile Ala Val Gln Gly Ala Glu Leu Ile Lys Thr Val Asp Ile Glu Glu Ala Asp Pro Pro Gln Leu Gly Asp Phe Thr Lys Asp Trp Val Glu Tyr Asn Cys Asn Ser Ser Asn Asn Ile Cys Trp Thr Glu Lys Gly Arg Thr Val Lys Ala Val Tyr Gly Val Ser Lys Arg Trp Ser Asp Tyr Thr Leu His Leu Pro Thr Gly Ser Asp Val Ala Lys His Trp Met Leu His Phe Pro Arg Ile Thr Tyr Pro Leu Val His Leu Ala Asn Trp Leu Cys Gly Leu Asn Leu Phe Trp Ile Cys Lys Thr Cys Phe Arg Cys Leu Lys Arg Leu Lys Met Ser Trp Phe Leu Pro Thr Val Leu Asp Thr 

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Gly Gln Gly Phe Lys Leu Val Lys Ser

690 695

<210> 78

<211> 3008

<212> DNA

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<220>

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<222> (372)..(2462)

1

<400> 78

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aaagtttacg ccgacactgg cctgtattag cgcgtatggc ctcgggccct cgttccccaa 120

ggcgtgccgc ctccctgttc tcagtcgcag gctgaagcct tgtctgctct cctcctttt 180

ggtttggttt tggaactgac tccgagggtt gggagagcgc gttggtggcg acggccgagt 240

cagatcacta taaacaaaat ttccacaaga gaaaatgttg aaataggagt tgcggataca 300

ttggatatac tggatgaaat acaagcggtt aatttttgta acgtgaggga aaagcccaca 360

ttgctggtta c atg tgt aaa tca ctg cgt tat tgc ttt agt cat tgt ctc 410

Met Cys Lys Ser Leu Arg Tyr Cys Phe Ser His Cys Leu

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10

5

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tat	tta	gca	atg	aca	aga	ctg	gaa	gaa	gta	aat	aga	gaa	gtg	aac	atg	458
Tyr	Leu	Ala	Met	Thr	Arg	Leu	Glu	Glu	Val	Asn	Arg	Glu	Val	Asn	Met	
	15					20					25					
cat	tct	tca	gtg	cgg	tat	ctt	ggc	tat	tta	gcc	aga	atc	aat	tta	ttg	506
His	Ser	Ser	Val	Arg	Tyr	Leu	Gly	Tyr	Leu	Ala	Arg	Ile	Asn	Leu	Leu	
30					35					40					45	
gtt	gct	ata	tgc	tta	ggt	cta	tac	gta	aga	tgg	gaa	aaa	aca	gca	aat	554
Val	Ala	Ile	Cys	Leu	Gly	Leu	Tyr	Val	Arg	Trp	Glu	Lys	Thr	Ala	Asn	
				50					55					60		
tcc	tta	att	ttg	gta	att	ttt	att	ctt	ggt	ctt	ttt	gtt	ctt	gga	atc	602
Ser	Leu	Ile	Leu	Val	Ile	Phe	Ile	Leu	Gly	Leu	Phe	Val	Leu	Gly	Ile	
			65					70					75			
gcc	agc	ata	ctc	tat	tac	tat	ttt	tca	atg	gaa	gca	gca	agt	tta	agt	650
Ala	Ser	Ile	Leu	Tyr	Tyr	Tyr	Phe	Ser	Met	Glu	Ala	Ala	Ser	Leu	Ser	
		80					85					90				
ctc	tcc	aat	ctt	tgg	ttt	gga	ttc	ttg	ctt	ggc	ctc	cta	tgt	ttt	ctt	698
Leu	Ser	Asn	Leu	Trp	Phe	Gly	Phe	Leu	Leu	Gly	Leu	Leu	Cys	Phe	Leu	
	95					100					105					
gat	aat	tca	tcc	ttt	aaa	aat	gat	gta	aaa	gaa	gaa	tca	acc	aaa	tat	746
Asp	Asn	Ser	Ser	Phe	Lys	Asn	Asp	Val	Lys	Glu	Glu	Ser	Thr	Lys	Tyr	
110					115					120					125	
ttg	ctt	cta	aca	tcc	ata	gtg	tta	agg	ata	ttg	tgc	tct	ctg	gtg	gag	794

Leu Leu Leu Thr Ser Ile Val Leu Arg Ile Leu Cys Ser Leu Val Glu aga att tet ggt tat gte egt eat egg eec act tta eta ace aca gtt Arg Ile Ser Gly Tyr Val Arg His Arg Pro Thr Leu Leu Thr Thr Val gaa ttt ctg gag ctt gtt gga ttt gcc att gcc agc aca act atg ttg Glu Phe Leu Glu Leu Val Gly Phe Ala Ile Ala Ser Thr Thr Met Leu gtg gag aag tot otg agt gto att ttg ott gta got otg got atg Val Glu Lys Ser Leu Ser Val Ile Leu Leu Val Val Ala Leu Ala Met ctg att att gat ctg aga atg aaa tct ttc tta gct att cca aac tta Leu Ile Ile Asp Leu Arg Met Lys Ser Phe Leu Ala Ile Pro Asn Leu gtt att ttt gca gtt ttg tta ttt ttt tcc tca ttg gaa act ccc aaa Val Ile Phe Ala Val Leu Leu Phe Phe Ser Ser Leu Glu Thr Pro Lys aat ccg att gct ttt gcg tgt ttt ttt att tgc ctg ata act gat cct Asn Pro Ile Ala Phe Ala Cys Phe Phe Ile Cys Leu Ile Thr Asp Pro ttc ctt gac att tat ttt agt gga ctt tca gta act gaa aga tgg aaa Phe Leu Asp Ile Tyr Phe Ser Gly Leu Ser Val Thr Glu Arg Trp Lys 266/735

		240					245					250				
ccc	ttt	ttg	tac	cgt	gga	aga	att	tgc	aga	aga	ctt	tca	gtc	gtt	ttt	1178
Pro	Phe	Leu	Tyr	Arg	Gly	Arg	Ile	Cys	Arg	Arg	Leu	Ser	Val	Val	Phe	
	255					260					265					
gct	gga	atg	att	gag	ctt	aca	ttt	ttt	att	ctt	tcc	gca	ttc	aaa	ctt	1226
Ala	Gly	Met	Ile	Glu	Leu	Thr	Phe	Phe	Ile	Leu	Ser	Ala	Phe	Lys	Leu	
270					275					280					285	
aga	gac	act	cac	ctc	tgg	tat	ttt	gta	ata	cct	ggc	ttt	tcc	att	ttt	1274
Arg	Asp	Thr	His	Leu	Trp	Tyr	Phe	Val	Ile	Pro	Gly	Phe	Ser	Ile	Phe	
				290					295					300		
gga	att	ttc	tgg	atg	att	tgt	cat	att	att	ttt	ctt	tta	act	ctt	tgg	1322
Gly	Ile	Phe	Trp	Met	Ile	Cys	His	Ile	Ile	Phe	Leu	Leu	Thr	Leu	Trp	
			305					310					315			
gga	ttc	cat	acc	aaa	tta	aat	gac	tgc	cat	aaa	gta	tat	ttt	act	cac	1370
Gly	Phe	His	Thr	Lys	Leu	Asn	Asp	Cys	His	Lys	Val	Tyr	Phe	Thr	His	
		320					325					330				
									•							
agg	aca	gat	tac	aat	agc	ctt	gat	aga	atc	atg	gca	tcc	aaa	ggg	atg	1418
Arg	Thr	Asp	Tyr	Asn	Ser	Leu	Asp	Arg	Ile	Met	Ala	Ser	Lys	Gly	Met	
	335					340					345					
	cat															1466
	His	Phe	Cys	Leu		Ser	Glu	Gln	Leu		Phe	Phe	Ser	Leu		
350					355			267/	735	360					365	
								-511								

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gca	aca	gcg	att	ttg	gga	gca	gtt	tcc	tgg	cag	cca	aca	aat	gga	att	1514
Ala	Thr	Ala	Ile	Leu	Gly	Ala	Val	Ser	Trp	Gln	Pro	Thr	Asn	Gly	Ile	
			•	370					375					380	٠	
ttc	ttg	agc	atg	ttt	cta	atc	gtt	ttg	cca	ttg	gaa	tcc	atg	gct	cat	1562
Phe	Leu	Ser	Met	Phe	Leu	Ile	Val	Leu	Pro	Leu	Glu	Ser	Met	Ala	His	
			385					390					395			
ggg	ctc	ttc	cat	gaa	ttg	ggt	aac	tgt	tta	gga	gga	aca	tct	gtt	gga	1610
G1y	Leu	Phe	His	Glu	Leu	Gly	Asn	Cys	Leu	Gly	Gly	Thr	Ser	Val	Gly	
		400					405					410				
tat	gct	att	gtg	att	ссс	acc	aac	ttc	tgc	agt	cct	gat	ggt	cag	cca	1658
Tyr	Ala	Ile	Val	Ile	Pro	Thr	Asn	Phe	Cys	Ser	Pro	Asp	Gly	Gln	Pro	
	415					420					425					
aca	ctg	ctt	ссс	cca	gaa	cat	gta	cag	gag	tta	aat	ttg	agg	tct	act	1706
Thr	Leu	Leu	Pro	Pro	Glu	His	·Val	G1n	Glu	Leu	Asn	Leu	Arg	Ser	Thr	
430					435					440					445	
ggc	atg	ctc	aat	gct	atc	caa	aga	ttt	ttt	gca	tat	cat	atg	att	gag	1754
Gly	Met	Leu	Asn	Ala	Ile	G1n	Arg	Phe	Phe	Ala	Tyr	His	Met	Ile	Glu	
				450					<b>4</b> 55					<b>46</b> 0		
acc	tat	gga	tgt	gac	tat	tcc	aca	agt	gga	ctg	tca	ttt	gat	act	ctg	1802
Thr	Tyr	Gly	Cys	Asp	Tyr	Ser	Thr	Ser	Gly	Leu	Ser	Phe	Asp	Thr	Leu	
			465					470					475			

cat tcc aaa cta aaa gct ttc ctc gaa ctt cgg aca gtg gat gga ccc 1850

His	Ser	Lys 480	Leu	Lys	Ala	Phe	Leu 485	Glu	Leu	Arg	Thr	Val 490	Asp	Gly	Pro	
		gat Asp														1898
		tgg Trp														1946
		tgg Trp														1994
		tta Leu														2042
		aat Asn 560														2090
		gat Asp														2138
aaa	gac	tgg	gta	gaa	tat	aac	tgc	aac 269/		agt	aat	aac	atc	tgc	tgg	2186

Lys	Asp	Trp	Val	G1u	Tyr	Asn	Cys	Asn	Ser	Ser	Asn	Asn	Ile	Cys	Trp	
590					595					600					605	
act	gaa	aag	gga	cgc	aca	gtg	aaa	gca	gta	tat	ggt	gtg	tca	aaa	cgg	2234
Thr	Glu	Lys	Gly	Arg	Thr	Val	Lys	Ala	Val	Tyr	Gly	Val	Ser	Lys	Arg	
				610					615					620		
tgg	agt	gac	tac	act	ctg	cat	ttg	cca	acg	gga	agc	gat	gtg	gcc	aag	2282
Trp	Ser	Asp	Tyr	Thr	Leu	His	Leu	Pro	Thr	Gly	Ser	Asp	Val	Ala	Lys	
			625					630					635			
cac	tgg	atg	tta	cac	ttt	cct	cgt	att	aca	tat	ссс	cta	gtg	cat	ttg	2330
His	Trp	Met	Leu	His	Phe	Pro	Arg	Ile	Thr	Tyr	Pro	Leu	Val	His	Leu	
		640					645					650				
gca	aat	tgg	tta	tgc	ggt	ctg	aac	ctt	ttt	tgg	atc	tgc	aaa	act	tgt	2378
Ala	Asn	Trp	Leu	Cys	Gly	Leu	Asn	Leu	Phe	Trp	Ile	Cys	Lys	Thr	Cys	
	655					660					665					
ttt	agg	tgc	ttg	aaa	aga	tta	aaa	atg	agt	tgg	ttt	ctt	cct	act	gtg	2426
Phe	Arg	Cys	Leu	Lys	Arg	Leu	Lys	Met	Ser	Trp	Phe	Leu	Pro	Thr	Val	
670					675					680					685	
ctg	gac	aca	gga	caa	ggc	ttc	aaa	ctt	gtc	aaa	tct	taat	ttgg	ac		2472
Leu	Asp	Thr	Gly	Gln	Gly	Phe	Lys	Leu	Val	Lys	Ser					
				690					695							

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gtatgctgta tttttatttg tggaaaatac cttgctactt ctgtagctgc tctcactttg 2592
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tggtcaatga tgaattacta atgccttatt ttctaggcat ataataatag tttagagaat 2832
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ctttttcca aacagtaggt ttcatccaag accatttgaa gaactgcaaa ctctttctct 2952
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<211> 611

<212> PRT

<213> Homo sapiens

<400> 79

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1 5 10 15

Leu Gly Leu Leu Cys Phe Leu Asp Asn Ser Ser Phe Lys Asn Asp Val
20 25 30

Lys	Glu	Glu	Ser	Thr	Lys	Tyr	Leu	Leu	Leu	Thr	Ser	Ile	Val	Leu	Arg
		35					40					45			
						-									
Ile	Leu	Cys	Ser	Leu	Val	Glu	Arg	Ile	Ser	Gly	Tyr	Val	Arg	His	Arg
	50					55					60				
Pro	Thr	Leu	Leu	Thr	Thr	Val	Glu	Phe	Leu	Glu	Leu	Val	Gly	Phe	Ala
65					70					75					80
Ile	Ala	Ser	Thr	Thr	Met	Leu	Val	Glu	Lys	Ser	Leu	Ser	Val	Ile	Leu
				85					90					95	
Leu	Val	Val	Ala	Leu	Ala	Met	Leu	Ile	Ile	Asp	Leu	Arg	Met	Lys	Ser
			100					105					110		
Phe	Leu	Ala	Ile	Pro	Asn	Leu	Val	Ile	Phe	Ala	Val	Leu	Leu	Phe	Phe
		115					120					125			
										_					
Ser		Leu	Glu	Thr	Pro		Asn	Pro	Ile	Ala		Ala	Cys	Phe	Phe
	130					135					140				•
	0 .	7	7.1	an i		n.	DI	7	<b>4</b>	T1 -	Т	Di	C	03-	T
	Cys	Leu	Ile	Inr		Pro	Phe	Leu	Asp		lyr	Phe	Ser	Gly	
145					150					155					160
So=	Vol	Thr	Glu	A~~	Тъъ	Lvc	Dro	Dho	Len	Tur	Δ <b>.</b>	G1 ···	Ar~	T1.	Cvc
ser	AST	IIII.	GIU	_	ırp	LYS	LLO	LIIG	170	TÀT	urg	GIÄ	vt. R	175	oys:
				165					110					110	

Arg Arg Leu Ser Val Val Phe Ala Gly Met Ile Glu Leu Thr Phe Phe

180

185

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190

Ile	Leu	Ser 195	Ala	Phe	Lys	Leu	Arg 200	Asp	Thr	His	Leu	Trp 205	Tyr	Phe	Va]
Ile	Pro 210	Gly	Phe	Ser	Ile	Phe 215	Gly	Ile	Phe	Trp	Met 220	Ile	Cys	His	Ile
Ile 225	Phe	Leu	Leu	Thr	Leu 230	Trp	Gly	Phe	His	Thr 235	Lys	Leu	Asn	Asp	Cys 240
His	Lys	Val	Tyr	Phe 245	Thr	His	Arg	Thr	Asp 250	Tyr	Asn	Ser	Leu	Asp 255	Arg
Ile	Met	Ala	Ser 260	Lys	Gly	Met	Arg	His 265	Phe	Cys	Leu	Ile	Ser 270	Glu	Glr
Leu	Val	Phe 275	Phe	Ser	Leu	Leu	Ala 280	Thr	Ala	Ile	Leu	Gly 285	Ala	Val	Ser
Trp	G1n 290	Pro	Thr	Asn	Gly	Ile 295	Phe	Leu	Ser	Met	Phe 300	Leu	Ile	Val	Leu
Pro 305	Leu	Glu	Ser	Met	Ala 310	His	Gly	Leu	Phe	His 315	Glu	Leu	Gly	Asn	Cys
Leu	Gly	Gly	Thr	Ser 325	Val	Gly	Tyr	Ala	Ile 330	Val	Ile	Pro	Thr	Asn 335	Phe

Cys Ser Pro Asp Gly Gln Pro Thr Leu Leu Pro Pro Glu His Val Gln 273/735

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350

Glu Leu Asn Leu Arg Ser Thr Gly Met Leu Asn Ala Ile Gln Arg Phe 355 360 365

345

340

Phe Ala Tyr His Met Ile Glu Thr Tyr Gly Cys Asp Tyr Ser Thr Ser 370 375 380

Gly Leu Ser Phe Asp Thr Leu His Ser Lys Leu Lys Ala Phe Leu Glu 385 390 395 400

Leu Arg Thr Val Asp Gly Pro Arg His Asp Thr Tyr Ile Leu Tyr Tyr
405 410 415

Ser Gly His Thr His Gly Thr Gly Glu Trp Ala Leu Ala Gly Gly Asp 420 425 430

Thr Leu Arg Leu Asp Thr Leu Ile Glu Trp Trp Arg Glu Lys Asn Gly
435
440
445

Ser Phe Cys Ser Arg Leu Ile Ile Val Leu Asp Ser Glu Asn Ser Thr 450 455 460

Pro Trp Val Lys Glu Val Arg Lys Ile Asn Asp Gln Tyr Ile Ala Val 465 470 475 480

Gln Gly Ala Glu Leu Ile Lys Thr Val Asp Ile Glu Glu Ala Asp Pro 485 490 495

Pro Gln Leu Gly Asp Phe Thr Lys Asp Trp Val Glu Tyr Asn Cys Asn 500 505 510

Ser Ser Asn Asn Ile Cys Trp Thr Glu Lys Gly Arg Thr Val Lys Ala 515 520 525

Val Tyr Gly Val Ser Lys Arg Trp Ser Asp Tyr Thr Leu His Leu Pro 530 535 540

Thr Gly Ser Asp Val Ala Lys His Trp Met Leu His Phe Pro Arg Ile 545 550 555 560

Thr Tyr Pro Leu Val His Leu Ala Asn Trp Leu Cys Gly Leu Asn Leu 565 570 575

Phe Trp Ile Cys Lys Thr Cys Phe Arg Cys Leu Lys Arg Leu Lys Met 580 585 590

Ser Trp Phe Leu Pro Thr Val Leu Asp Thr Gly Gln Gly Phe Lys Leu
595 600 605

Val Lys Ser 610

<210> 80

<211> 3007

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (629)..(2461)

<400> 80

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1

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5

tcc	aat	ctt	tgg	ttt	gga	ttc	ttg	ctt	ggc	ctc	cta	tgt	ttt	ctt	gat	700
Ser	Asn	Leu	Trp	Phe	Gly	Phe	Leu	Leu	Gly	Leu	Leu	Cys	Phe	Leu	Asp	
	10					15					20					
aat	tca	tcc	ttt	aaa	aat	gat	gta	aaa	gaa	gaa	tca	acc	aaa	tat	ttg	748
Asn	Ser	Ser	Phe	Lys	Asn	Asp	Val	Lys	Glu	Glu	Ser	Thr	Lys	Tyr	Leu	
25					30					35					40	
ctt	cta	aca	tcc	ata	gtg	tta	agg	ata	ttg	tgc	tct	ctg	gtg	gag	aga	796
Leu	Leu	Thr	Ser	Ile	Val	Leu	Arg	Ile	Leu	Cys	Ser	Leu	Val	Glu	Arg	
				45					50					55		
att	tct	ggt	tat	gtc	cgt	cat	cgg	ccc	act	tta	cta	acc	aca	gtt	gaa	844
Ile	Ser	Gly	Tyr	Val	Arg	His	Arg	Pro	Thr	Leu	Leu	Thr	Thr	Val	Glu	
			60					65					70			
ttt	ctg	gag	ctt	gtt	gga	ttt	gcc	att	gcc	agc	aca	act	atg	ttg	gtg	892
Phe	Leu	G1u	Leu	Val	Gly	Phe	Ala	Ile	Ala	Ser	Thr	Thr	Met	Leu	Val	
		<b>7</b> 5					80					85				
gag	aag	tct	ctg	agt	gtc	att	ttg	ctt	gtt	gta	gct	ctg	gct	atg	ctg	940
Glu	Lys	Ser	Leu	Ser	Val	Ile	Leu	Leu	Val	Val	Ala	Leu	Ala	Met	Leu	
	90					95					100					
att	att	gat	ctg	aga	atg	aaa	tct	ttc	tta	gct	att	cca	aac	tta	gtt	988
[le	Ile	Asp	Leu	Arg	Met	Lys	Ser	Phe	Leu	Ala	Ile	Pro	Asn	Leu	Val	
105					110					115				•	120	

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	att	ttt	gca	gtt	ttg	tta	ttt	ttt	tcc	tca	ttg	gaa	act	ccc	aaa	aat	1036
	Ile	Phe	Ala	Val	Leu	Leu	Phe	Phe	Ser	Ser	Leu	Glu	Thr	Pro	Lys	Asn	
					125					130					135		
	ccg	att	gct	ttt	gcg	tgt	ttt	ttt	att	tgc	ctg	ata	act	gat	cct	ttc	1084
	Pro	Ile	Ala	Phe	Ala	Cys	Phe	Phe	Ile	Cys	Leu	Ile	Thr	Asp	Pro	Phe	
				140					145					150			
	ctt	gac	att	tat	ttt	agt	gga	ctt	tca	gta	act	gaa	aga	tgg	aaa	ссс	1132
	Leu	Asp	Ile	Tyr	Phe	Ser	Gly	Leu	Ser	Val	Thr	Glu	Arg	Trp	Lys	Pro	
			155					160					165				
	ttt	ttg	tac	cgt	gga	aga	att	tgc	aga	aga	ctt	tca	gtc	gtt	ttt	gct	1180
	Phe	Leu	Tyr	Arg	Gly	Arg	Ile	Cys	Arg	Arg	Leu	Ser	Val	Val	Phe	Ala	
		170					175					180					
•	gga	atg	att	gag	ctt	aca	ttt	ttt	att	ctt	tcc	gca	ttc	aaa	ctt	aga	1228
	Gly	Met	Ile	Glu	Leu	Thr	Phe	Phe	Ile	Leu	Ser	Ala	Phe	Lys	Leu	Arg	
	185					190					195					200	
	gac	act	cac	ctc	tgg	tat	ttt	gta	ata	cct	ggc	ttt	tcc	att	ttt	gga	1276
	Asp	Thr	His	Leu	Trp	Tyr	Phe	Val	Ile	Pro	Gly	Phe	Ser	Ile	Phe	Gly	
					205					210					215		
	att	ttc	tgg	atg	att	tgt	cat	att	att	ttt	ctt	tta	act	ctt	tgg	gga	1324
	Ile	Phe	Trp	Met	Ile	Cys	His	Ile	Ile	Phe	Leu	Leu	Thr	Leu	Trp	Gly	
				220					225		•			230			
	ttc	cat	acc	aaa	tta	aat	gac	tgc	cat 278/		gta	tat	ttt	act	cac	agg	1372
									4101	, ,,							

Phe His Thr Lys Leu Asn Asp Cys His Lys Val Tyr Phe Thr His Arg aca gat tac aat agc ctt gat aga atc atg gca tcc aaa ggg atg cgc Thr Asp Tyr Asn Ser Leu Asp Arg Ile Met Ala Ser Lys Gly Met Arg cat ttt tgc ttg att tca gag cag ttg gtg ttc ttt agt ctt ctt gca His Phe Cys Leu Ile Ser Glu Gln Leu Val Phe Phe Ser Leu Leu Ala aca gcg att ttg gga gca gtt tcc tgg cag cca aca aat gga att ttc Thr Ala Ile Leu Gly Ala Val Ser Trp Gln Pro Thr Asn Gly Ile Phe ttg agc atg ttt cta atc gtt ttg cca ttg gaa tcc atg gct cat ggg Leu Ser Met Phe Leu Ile Val Leu Pro Leu Glu Ser Met Ala His Gly ctc ttc cat gaa ttg ggt aac tgt tta gga gga aca tct gtt gga tat Leu Phe His Glu Leu Gly Asn Cys Leu Gly Gly Thr Ser Val Gly Tyr gct att gtg att ccc acc aac ttc tgc agt cct gat ggt cag cca aca Ala Ile Val Ile Pro Thr Asn Phe Cys Ser Pro Asp Gly Gln Pro Thr ctg ctt ccc cca gaa cat gta cag gag tta aat ttg agg tct act ggc Leu Leu Pro Pro Glu His Val Gln Glu Leu Asn Leu Arg Ser Thr Gly 279/735

345					350					355					360	
atg	ctc	aat	gct	atc	caa	aga	ttt	ttt	gca	tat	cat	atg	att	gag	acc	1756
Met	Leu	Asn	Ala	Ile	Gln	Arg	Phe	Phe	Ala	Tyr	His	Met	Ile	Glu	Thr	
				365					370					375		
tat	gga	tgt	gac	tat	tcc	aca	agt	gga	ctg	tca	ttt	gat	act	ctg	cat	1804
Tyr	Gly	Cys	Asp	Tyr	Ser	Thr	Ser	Gly	Leu	Ser	Phe	Asp	Thr	Leu	His	
	٠		380					385					390			
tcc	aaa	cta	aaa	gct	ttc	ctc	gaa	ctt	cgg	aca	gtg	gat	gga	ccc	aga	1852
Ser	Lys	Leu	Lys	Ala	Phe	Leu	G1u	Leu	Arg	Thr	Val	Asp	Gly	Pro	Arg	
		395					400					405				
cat	gat	acg	tat	att	ttg	tat	tac	agt	ggg	cac	acc	cat	ggt	aca	gga	1900
His	Asp	Thr	Tyr	Ile	Leu	Tyr	Tyr	Ser	Gly	His	Thr	His	Gly	Thr	Gly	
	410					415					420					
gag	tgg	gct	cta	gca	ggt	gga	gat	aca	cta	cgc	ctt	gac	aca	ctt	ata	1948
G1u	Trp	Ala	Leu	Ala	Gly	Gly	Asp	Thr	Leu	Arg	Leu	Asp	Thr	Leu	Ile	
425					430					435					440	
gaa	tgg	tgg	aga	gaa	aag	aat	ggt	tcc	ttt	tgt	tcc	cgg	ctt	att	atc	1996
Glu	Trp	Trp	Arg	Glu	Lys	Asn	G1y	Ser	Phe	Cys	Ser	Arg	Leu	Ile	Ile	
				445					450					455		
gta	tta	gac	agc	gaa	aat	tca	acc	cct	tgg	gtg	aaa	gaa	gtg	agg	aaa	2044
Val	Leu	Asp	Ser	G1u	Asn	Ser	Thr	Pro	Trp	Val	Lys	Glu	Val	Arg	Lys	
			460					465					470			

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att aat gac cag tat att gca gtg caa gga gca gag ttg ata aaa aca Ile Asn Asp Gln Tyr Ile Ala Val Gln Gly Ala Glu Leu Ile Lys Thr gta gat att gaa gaa gct gac ccg cca cag cta ggt gac ttt aca aaa Val Asp Ile Glu Glu Ala Asp Pro Pro Gln Leu Gly Asp Phe Thr Lys gac tgg gta gaa tat aac tgc aac tcc agt aat aac atc tgc tgg act Asp Trp Val Glu Tyr Asn Cys Asn Ser Ser Asn Asn Ile Cys Trp Thr gaa aag gga cgc aca gtg aaa gca gta tat ggt gtg tca aaa cgg tgg Glu Lys Gly Arg Thr Val Lys Ala Val Tyr Gly Val Ser Lys Arg Trp agt gac tac act ctg cat ttg cca acg gga agc gat gtg gcc aag cac Ser Asp Tyr Thr Leu His Leu Pro Thr Gly Ser Asp Val Ala Lys His tgg atg tta cac ttt cct cgt att aca tat ccc cta gtg cat ttg gca Trp Met Leu His Phe Pro Arg Ile Thr Tyr Pro Leu Val His Leu Ala 

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aat tgg tta tgc ggt ctg aac ctt ttt tgg atc tgc aaa act tgt ttt

Asn Trp Leu Cys Gly Leu Asn Leu Phe Trp Ile Cys Lys Thr Cys Phe

agg tgc ttg aaa aga tta aaa atg agt tgg ttt ctt cct act gtg ctg 2428

Arg Cys Leu Lys Arg Leu Lys Met Ser Trp Phe Leu Pro Thr Val Leu

585 590 595 600

gac aca gga caa ggc ttc aaa ctt gtc aaa tct taatttggac cccaaagcgg 2481 Asp Thr Gly Gln Gly Phe Lys Leu Val Lys Ser

605 610

gatattaata agcactcata ctaccaatta tcactaactt gccattttt gtatgctgta 2541

tttttatttg tggaaaatac cttgctactt ctgtagctgc tctcactttg tctttctta 2601

agtaattatg gtatatataa ggcgttggga aaaaacattt tataatgaaa gtatgtaggg 2661

agtcaaatgc ttactgtaaa tgcataagag acgttaaaaa taacactgca ctttcaggaa 2721

tgtttgctta tggtcctgat tagaaagaaa cagttgtcta tgctctgcaa tggtcaatga 2781

tgaattacta atgccttatt ttctaggcat ataataatag tttagagaat gtagaccaga 2841

taaatttgtt tactgttta agaaaactac cagtttactt acagaagatt ctttttcca 2901

aacagtaggt ttcatccaag accatttgaa gaactgcaaa ctctttctct tagaaaagaa 2961

agagggcagc ctaaaataaa cgcaaaattt gcttatactc catcac 3007

<210> 81

<211> 184

<212> PRT

<213> Homo sapiens.

<400> 81

Met Thr Ser Phe Glu Asp Ala Asp Thr Glu Glu Thr Val Thr Cys Leu

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Gln Met Thr Val Tyr His Pro Gly Gln Leu Gln Cys Gly Ile Phe Gln
20 25 30

Ser Ile Ser Phe Asn Arg Glu Lys Leu Pro Ser Ser Glu Val Val Lys
35 40 45

Phe Gly Arg Asn Ser Asn Ile Cys His Tyr Thr Phe Gln Asp Lys Gln
50 55 60

Val Ser Arg Val Gln Phe Ser Leu Gln Leu Phe Lys Lys Phe Asn Ser
65 70 75 80

Ser Val Leu Ser Phe Glu Ile Lys Asn Met Ser Lys Lys Thr Asn Leu 85 90 95

Ile Val Asp Ser Arg Glu Leu Gly Tyr Leu Asn Lys Met Asp Leu Pro
100 105 110

Tyr Arg Cys Met Val Arg Phe Gly Glu Tyr Gln Phe Leu Met Glu Lys
115 120 125

Glu Asp Gly Glu Ser Leu Glu Phe Phe Glu Thr Gln Phe Ile Leu Ser 283/735

130 135 140

Pro Arg Ser Leu Leu Gln Glu Asn Asn Trp Pro Pro His Arg Pro Ile 145 150 155 160

Pro Glu Tyr Gly Thr Tyr Ser Leu Cys Ser Ser Gln Ser Ser Pro 165 170 175

Thr Glu Met Asp Glu Asn Glu Ser 180

<210> 82

<211> 1617

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (285).. (836)

<400> 82

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ccgcaccccg gggctcacac ttacccgcgc ggaggagcag cggccgggtg tccacccca 180

tectgegeec agtetecteg atteceeteg etetgageeg ggagageega acagetgaag 240 284/735

agagttcact gactccccag ccccaggtgg gccttgtgca catc atg acc agt ttt 296

Met Thr Ser Phe

1

gaa gat gct gac aca gaa gag aca gta act tgt ctc cag atg acg gtt 344
Glu Asp Ala Asp Thr Glu Glu Thr Val Thr Cys Leu Gln Met Thr Val
5 10 15 20

tac cat cct ggc cag ttg cag tgt gga ata ttt cag tca ata agt ttt 392

Tyr His Pro Gly Gln Leu Gln Cys Gly Ile Phe Gln Ser Ile Ser Phe

25 30 35

aac aga gag aaa ctc cct tcc agc gaa gtg gtg aaa ttt ggc cga aat 440 Asn Arg Glu Lys Leu Pro Ser Ser Glu Val Val Lys Phe Gly Arg Asn 40 45 50

tcc aac atc tgt cat tat act ttt cag gac aaa cag gtt tcc cga gtt 488
Ser Asn Ile Cys His Tyr Thr Phe Gln Asp Lys Gln Val Ser Arg Val
55 60 65

cag ttt tct ctg cag ctg ttt aaa aaa ttc aac agc tca gtt ctc tcc 536
Gln Phe Ser Leu Gln Leu Phe Lys Lys Phe Asn Ser Ser Val Leu Ser
70 75 80

ttt gaa ata aaa aat atg agt aaa aag acc aat ctg atc gtg gac agc 584

Phe Glu Ile Lys Asn Met Ser Lys Lys Thr Asn Leu Ile Val Asp Ser

85 90 95 100

aga	gag	ctg	ggc	tac	cta	aat	aaa	atg	gac	ctg	cca	tac	agg	tgc	atg	632
Arg	Glu	Leu	Gly	Tyr	Leu	Asn	Lys	Met	Asp	Leu	Pro	Tyr	Arg	Cys	Met	
				105					110					115	•	
gtc	aga	ttc	gga	gag	tat	cag	ttt	ctg	atg	gag	aag	gaa	gat	ggc	gag	680
Val	Arg	Phe	Gly	Glu	Tyr	Gln	Phe	Leu	Met	Glu	Lys	Glu	Asp	Gly	Glu	
			120					125					130			
tca	ttg	gaa	ttt	ttt	gag	act	caa	ttt	att	tta	tct	cca	aga	tca	ctc	728
Ser	Leu	Glu	Phe	Phe	Glu	Thr	Gln	Phe	Ile	Leu	Ser	Pro	Arg	Ser	Leu	
		135					140					145				
ttg	caa	gaa	aac	aac	tgg	cca	cca	cac	agg	ccc	ata	ccg	gag	tat	ggc	776
Leu	Gln	Glu	Asn	Asn	Trp	Pro	Pro	His	Arg	Pro	Ile	Pro	Glu	Tyr	Gly	
	150					155					160					
act	tat	tcg	ctc	tgc	tcc	tcc	caa	agc	agt	tct	ccg	aca	gaa	atg	gat	824
Thr	Tyr	Ser	Leu	Cys	Ser	Ser	Gln	Ser	Ser	Ser	Pro	Thr	G1u	Met	Asp	
165					170					175					180	
gaa	aat	gag	tca	tgaa	icaca	aga a	agto	taag	a gg	gagaa	atat	gat	gga	tgaa		876
Glu	Asn	G1u	Ser													
gago	tcte	gta g	gatgo	tgta	it ag	gacac	taaa	taa	gagt	tga	ttag	ggta	ıgt a	atatt	atagt	936
cato	tgtt	at g	ctgt	gaaa	it tt	ggaa	ttca	gta	ttat	cat	tttg	aagt	ct g	gtaaa	ttgtg	996
	-		_	-		-						_				
ttag	tcat	ta a	ictta	igtca	ıc ct	gtte	tatt	cte	gato	tac	acaa	aatt	at t	tttaa	ctgct	1056
				_				_	-						J	- •

cttattaatc tgtgaggatt aatatacaaa aagtatcctt tgagatgaag tcgtgttctc 1116

aaaataaggt tatattattt tctttttctg cttgatttc atcttgtgtt ttgctttgtt 1176

tttgtaagga accatctctt ggtttggtca catcagttca caacagccat ttgttttcaa 1236

ggtcaaggct ccaggcaggt tgttactggt gtttgcagcc tgtcagtact tgcagtactg 1296

gaataggttc taggctagtg tctgcgcgtc actgtggttt tagcatggga ggacttattt 1356

gagaaaatact accttacttt tctatgattt ctttttacag agttatagtg tgtttactcc 1416

taagatgaca gttctcttg tctatattca gcatctaaga caaatattta aacattttaa 1476

agaaccactg tgttaagttt aggattattt acttaccaaa ttagaagttt gactttattg 1536

tgttatacac aatcttaaaa tttcacgaat tcacctttt aatagtatcc atgtacataa 1596

taaaatcaaa gtttaattag c

<210> 83

<211> 392

<212> PRT

<213> Homo sapiens

<400> 83

Met Asp Ala Arg Trp Trp Ala Val Val Leu Ala Ala Phe Pro Ser

1 5 10 15

Leu	Gly	Ala	Gly	Gly	Glu	Thr	Pro	Glu	Ala	Pro	Pro	Glu	Ser	Trp	Thr
			20					25					30		
G1n	Leu	Trp	Phe	Phe	Arg	Phe	Val	Val	Asn	Ala	Ala	G1y	Tyr	Ala	Ser
		35					40					45			
Phe	Met	Val	Pro	Gly	Tyr	Leu	Leu	Val	Gln	Tyr	Phe	Arg	Arg	Lys	Asn
	50					<b>5</b> 5					60				
Tyr	Leu	G1u	Thr	G1y	Arg	G1y	Leu	Cys	Phe	Pro	Leu	Val	Lys	Ala	Cys
65					70					75					80
Val	Phe	Gly	Asn	Glu	Pro	Lys	Ala	Ser	Asp	Glu	Val	Pro	Leu	Ala	Pro
				85					90					95	
Arg	Thr	Glu	Ala	Ala	Glu	Thr	Thr	Pro	Met	Trp	G1n	Ala	Leu	Lys	Leu
			100					105					110		
Leu	Phe	Cys	Ala	Thr	Gly	Leu	Gln	Val	Ser	Tyr	Leu	Thr	Trp	Gly	Val
		115					120					125			
Leu	Gln	Glu	Arg	Val	Met	Thr	Arg	Ser	Tyr	Gly	Ala	Thr	Ala	Thr	Ser
	130					135					140				
Pro	Gly	G1u	Arg	Phe	Thr	Asp	Ser	Gln	Phe	Leu	Val	Leu	Met	Asn	Arg
145					150					155					160
Val	Leu	Ala	Leu	Ile	Val	Ala	Gly	Leu	Ser	Cys	Val	Leu	Cys	Lys	G1n

165 170 175

Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser 180 185 190

Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser 195 200 205

Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met 210 215 220

Leu Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr 225 230 235 240

Leu Thr Ala Thr Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser

245 250 255

Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu 260 265 270

Phe Thr Val Gly Ser Leu Leu Glu Gln Gly Ala Leu Leu Glu Gly Thr
275 280 285

Arg Phe Met Gly Arg His Ser Glu Phe Ala Ala His Ala Leu Leu Leu 290 295 300

Ser Ile Cys Ser Ala Cys Gly Gln Leu Phe Ile Phe Tyr Thr Ile Gly 305 310 315 320

Gln Phe Gly Ala Ala Val Phe Thr IIe IIe Met Thr Leu Arg Gln Ala 325 330 335

Phe Ala Ile Leu Leu Ser Cys Leu Leu Tyr Gly His Thr Val Thr Val
340 345 350

Val Gly Gly Leu Gly Val Ala Val Phe Ala Ala Leu Leu Leu Arg 355 360 365

Val Tyr Ala Arg Gly Arg Leu Lys Gln Arg Gly Lys Lys Ala Val Pro 370 375 380

Val Glu Ser Pro Val Gln Lys Val 385 390

<210> 84

<211> 1898

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (119).. (1294)

<400> 84

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cgcgcgccc ggggactcgc attccccggt tccccctcca ccccacgcgg cctggacc 118
290/735

atg	gac	gcc	aga	tgg	tgg	gca	gtg	gtg	gtg	ctg	gct	gcg	ttc	ccc	tcc	166
Met	Asp	Ala	Arg	Trp	Trp	Ala	Val	Val	Val	Leu	Ala	Ala	Phe	Pro	Ser	
1				5					10					15		
cta	ggg	gca	ggt	ggg	gag	act	ccc	gaa	gcc	cct	ccg	gag	tca	tgg	acc	214
Leu	Gly	Ala	Gly	Gly	Glu	Thr	Pro	Glu	Ala	Pro	Pro	Glu	Ser	Trp	Thr	
			20					25					30			
cag	cta	tgg	ttc	ttc	cga	ttt	gtg	gtg	aat	gct	gct	ggc	tat	gcc	agc	262
Gln	Leu	Trp	Phe	Phe	Arg	Phe	Val	Val	Asn	Ala	Ala	Gly	Tyr	Ala	Ser	
		35					40					45				
ttt	atg	gta	cct	ggc	tac	ctc	ctg	gtg	cag	tac	ttc	agg	cgg	aag	aac	310
Phe	Met	Val	Pro	Gly	Tyr	Leu	Leu	Val	Gln	Tyr	Phe	Arg	Arg	Lys	Asn	
	50					55					60					
tac	ctg	gag	acc	ggt	agg	ggc	ctc	tgc	ttt	ccc	ctg	gtg	aaa	gct	tgt	358
Tyr	Leu	Glu	Thr	Gly	Arg	Gly	Leu	Cys	Phe	Pro	Leu	Val	Lys	Ala	Cys	
65					70					75					80	
gtg	ttt	ggc	aat	gag	ccc	aag	gcc	tct	gat	gag	gtt	ccc	ctg	gcg	ccc	406
Val	Phe	Gly	Asn	G1u	Pro	Lys	Ala	Ser	Asp	Glu	Va1	Pro	Leu	Ala	Pro	
				85					90					95		
cga	aca	gag	gcg	gca	gag	acc	acc	ccg	atg	tgg	cag	gcc	ctg	aag	ctg	454
Arg	Thr	Glu	Ala	Ala	G1u	Thr	Thr	Pro	Met	Trp	Gln	A1a	Leu	Lys	Leu	
			100					105					110		٠	

	ctc	ttc	tgt	gcc	aca	ggg	ctc	cag	gtg	tct	tat	ctg	act	tgg	ggt	gtg	502
	Leu	Phe	Cys	Ala	Thr	Gly	Leu	Gln	Val	Ser	Tyr	Leu	Thr	Trp	Gly	Val	
			115					120	•				125				
	ctg	cag	gaa	aga	gtg	atg	acc	cgc	agc	tat	ggg	gcc	aca	gcc	aca	tca	550
	Leu	Gln	Glu	Arg	Val	Met	Thr	Arg	Ser	Tyr	G1y	Ala	Thr	Ala	Thr	Ser	
		130					135					140					
	ccg	ggt	gag	cgc	ttt	acg	gac	tcg	cag	ttc	ctg	gtg	cta	atg	aac	cga	598
	Pro	G1y	Glu	Arg	Phe	Thr	Asp	Ser	Gln	Phe	Leu	Val	Leu	Met	Asn	Arg	
	145					150					155					160	
	gtg	ctg	gca	ctg	att	gtg	gct	ggc	ctc	tcc	tgt	gtt	ctc	tgc	aag	cag	646
	Val	Leu	Ala	Leu	Ile	Val	Ala	Gly	Leu	Ser	Cys	Val	Leu	Cys	Lys	Gln	
					165					170					175		
	ссс	cgg	cat	ggg	gca	ссс	atg	tac	cgg	tac	tcc	ttt	gcc	agc	ctg	tcc	694
-	Pro	Arg	His	Gly	Ala	Pro	Met	Tyr	Arg	Tyr	Ser	Phe	Ala	Ser	Leu	Ser	
				180					185					190			
	aat	gtg	ctt	agc	agc	tgg	tgc	caa	tac	gaa	gct	ctt	aag	ttc	gtc	agc	742
	Asn	Val	Leu	Ser	Ser	Trp	Cys	Gln	Tyr	Glu	Ala	Leu	Lys	Phe	Val	Ser	
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	Phe	Pro	Thr	G1n	Val	Leu	Ala	Lys	Ala	Ser	Lys	Val	Ile	Pro	Val	Met	
		210					215					220					
	ctg	atg	gga	aag	ctt	gtg	tct	cgg	cgc		tac	gaa	cac	tgg	gag	tac	838
									292	ツマモ							

Leu	Met	GIY	Lys	Leu	Val	Ser	MIR	WLA	Ser	I y I	GIU	uis	IIp	GIU	I y I	
225					230					235					240	
ctg	aca	gcc	acc	ctc	atc	tcc	att	ggg	gtc	agc	atg	ttt	ctg	cta	tcc	886
Leu	Thr	Ala	Thr	Leu	Ile	Ser	Ile	Gly	Val	Ser	Met	Phe	Leu	Leu	Ser	
				245					250					255	•	
	-															
agc	gga	cca	gag	ссс	cgc	agc	tcc	cca	gcc	acc	aca	ctc	tca	ggc	ctc	934
Ser	Gly	Pro	Glu	Pro	Arg	Ser	Ser	Pro	Ala	Thr	Thr	Leu	Ser	Gly	Leu	
			260					265					270			
ttc	aca	gtg	ggc	tca	ctg	cta	gaa	cag	ggg	gcc	cta	ctg	gag	gga	acc	982
Phe	Thr	Val	Gly	Ser	Leu	Leu	Glu	Gln	Gly	Ala	Leu	Leu	Glu	Gly	Thr	
		275					280					285				
cgc	ttc	atg	ggg	cga	cac	agt	gag	ttt	gct	gcc	cat	gcc	ctg	cta	ctc	1030
Arg	Phe	Met	Gly	Arg	His	Ser	Glu	Phe	Ala	Ala	His	Ala	Leu	Leu	Leu	
	290					295					300					
tcc	atc	tgc	tcc	gca	tgt	ggc	cag	ctc	ttc	atc	ttt	tac	acc	att	ggg	1078
Ser	Ile	Cys	Ser	Ala	Cys	Ġly	G1n	Leu	Phe	Ile	Phe	Tyr	Thr	Ile	Gly	
305					310					315					320	
cag	ttt	ggg	gct	gcc	gtc	ttc	acc	atc	atc	atg	acc	ctc	cgc	cag	gcc	1126
Gln	Phe	Gly	Ala	Ala	Val	Phe	Thr	Ile	Ile	Met	Thr	Leu	Arg	Gln	Ala	
				325					330					335		
ttt	gcc	atc	ctt	ctt	tcc	tgc	ctt	ctc	tat	ggc	cac	act	gtc	act	gtg	1174
Phe	Ala	Ile	Leu	Leu	Ser	Cys	Leu	Leu	Tyr	Gly	His	Thr	Val	Thr	Val	
								293/	735							

340 345 350

gtc tac gcg cgg ggc cgt cta aag caa cgg gga aag aag gct gtg cct 1270

Val Tyr Ala Arg Gly Arg Leu Lys Gln Arg Gly Lys Lys Ala Val Pro
370 375 380

gtt gag tct cct gtg cag aag gtt tgagggtgga aagggcctga ggggtgaagt 1324 Val Glu Ser Pro Val Gln Lys Val 385 390

gaaataggac ceteccaca teceettetg etgtaacete tgagggaget ggetgaaagg 1384
gcaaaatgca ggtgtttet cagtateaca gaccagetet gcagcagggg attggggage 1444
ccaggaggca gcettecett ttgeettaag teaceeatet tecagtaage agtttattet 1504
gageeeeggg ggtagacagt ceteagtgag gggttttggg gagtttgggg teaagagage 1564
ataggtaggt teeacagtta etetteecac aagtteeett aagtettgee etagetgge 1624
tetgeeacet teeagaetea eteeeeteg caaatacetg catttettae eetggtgaga 1684
aaageacaag eggtgtagge teeaatgetg ettteecagg agggtgaaga tggtgetgtg 1744
ctgaggaaag gggatgeaga geeetgeeea geaceaceae eteetatget eetggateee 1804
294/735

taggetetgt tecatgagee tgttgeaggt tttggtaett tagaaatgta aetttttget 1864

cttataattt tattttatta aattaaatta ctgc

1898

<210> 85

<211> 432

<212> PRT

<213> Homo sapiens

<400> 85

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Leu Gly Ala Gly Gly Glu Thr Pro Glu Ala Pro Pro Glu Ser Trp Thr
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Gln Leu Trp Phe Phe Arg Phe Val Val Asn Ala Ala Gly Tyr Ala Ser 35 40 . 45

Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Phe Arg Arg Lys Asn 50 55 60

Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys
65 70 75 80

Val Phe Gly Asn Glu Pro Lys Ala Ser Asp Glu Val Pro Leu Ala Pro
85 90 95
295/735

Arg	Thr	G1u	Ala 100	Ala	G1u	Thr	Thr	Pro 105	Met	Trp	Gln	Ala	Leu 110	Lys	Leu
Leu	Phe	Cys 115	Ala	Thr	Gly	Leu	Gln 120	Val	Ser	Tyr	Leu	Thr 125	Trp	Gly	Val
Leu	Gln 130	Glu	Arg	Val	Met	Thr 135	Arg	Ser	Tyr	Gly	Ala 140	Thr	Ala	Thr	Ser
Pro 145	G1y	Glu	Arg	Phe	Thr 150	Asp	Ser	Gln	Phe	Leu 155	Val	Leu	Met	Asn	Arg 160
Val	Leu	Ala	Leu	Ile 165	Val	Ala	G1y	Leu	Ser 170	Cys	Val	Leu	Cys	Lys 175	G1n
Pro	Arg	His	Gly 180	Ala	Pro	Met	Tyr	Arg 185	Tyr	Ser	Phe	Ala	Ser 190	Leu	Ser
Asn	Val	Leu 195	Ser	Ser	Trp	Cys	Gln 200	Tyr	Glu	Ala	Leu	Lys 205	Phe .	Val	Ser
Phe	Pro 210	Thr	Gln	Val	Leu	Ala 215	Lys	Ala	Ser	Lys	Val 220	Ile	Pro	Val	Met
Leu 225	Met	Gly	Lys	Leu	Val 230	Ser	Arg	Arg	Ser	Tyr 235	G1u	His	Trp	Glu	Tyr 240

Leu Thr Ala Thr Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser

WO 02/053737			PCT/JP01/11389
	245	250	255

Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu 260 265 270

Ile Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp
275 280 285

Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe 290 295 300

Gly Val Asn Phe Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu
305 310 315 320

Gln Gly Ala Leu Leu Glu Gly Thr Arg Phe Met Gly Arg His Ser Glu 325 330 335

Phe Ala Ala His Ala Leu Leu Leu Ser Ile Cys Ser Ala Cys Gly Gln 340 345 350

Leu Phe Ile Phe Tyr Thr Ile Gly Gln Phe Gly Ala Ala Val Phe Thr
355 360 365

Ile Ile Met Thr Leu Arg Gln Ala Phe Ala Ile Leu Leu Ser Cys Leu 370 375 380

Leu Tyr Gly His Thr Val Thr Val Gly Gly Leu Gly Val Ala Val
385 390 395 400

Val Phe Ala Ala Leu Leu Leu Arg Val Tyr Ala Arg Gly Arg Leu Lys
405 410 415

Gln Arg Gly Lys Lys Ala Val Pro Val Glu Ser Pro Val Gln Lys Val
420 425 430

<210> 86

<211> 2018

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (119).. (1414)

20

<400> 86

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cgcgcggccc ggggactcgc attccccggt tccccctcca ccccacgcgg cctggacc 118

atg gac gcc aga tgg tgg gca gtg gtg gtg ctg gct gcg ttc ccc tcc 166

Met Asp Ala Arg Trp Trp Ala Val Val Leu Ala Ala Phe Pro Ser

1 5 10 15

cta ggg gca ggt ggg gag act ccc gaa gcc cct ccg gag tca tgg acc 214 Leu Gly Ala Gly Gly Glu Thr Pro Glu Ala Pro Pro Glu Ser Trp Thr

25

30

cag	cta	tgg	ttc	ttc	cga	ttt	gtg	gtg	aat	gct	gct	ggc	tat	gcc	agc	262
Gln	Leu	Trp	Phe	Phe	Arg	Phe	Val	Val	Asn	Ala	Ala	Gly	Tyr	Ala	Ser	
		35					40					45				
ttt	atg	gta	cct	ggc	tac	ctc	ctg	gtg	cag	tac	ttc	agg	cgg	aag	aac	310
Phe	Met	Val	Pro	Gly	Tyr	Leu	Leu	Val	Gln	Tyr	Phe	Arg	Arg	Lys	Asn	
	50					55					60					
tac	ctg	gag	acc	ggt	agg	ggc	ctc	tgc	ttt	ccc	ctg	gtg	aaa	gct	tgt	358
Tyr	Leu	Glu	Thr	Gly	Arg	Gly	Leu	Cys	Phe	Pro	Leu	Val	Lys	Ala	Cys	
65					70					75					80	
	ttt															406
Val	Phe.	Gly	Asn		Pro	Lys	Ala	Ser		Glu	Val	Pro	Leu		Pṛo	
				85					90					95		
	aca															454
Arg	Thr	GIU		Ата	GIU	ınr	Inr		мет	irp	GIN	Ala		Lys	Leu	
			100					105					110			
ctc	ttc	+ a+	geo.	9.09	aaa	ctc	cau	at a	tet	<b>+</b> 2+	c+a	20+	taa	aat	at a	502
	Phe															002
Deu	1 110	115	1114	1111	U1,	Dod	120		501	1,1	Dou	125	11,5	01)	, 42	
		110					-20					100				
ctg	cag	gaa	aga	gtg	ate	acc	cgc	agc	tat	ggg	gcc	aca	gcc	aca	tca	550
	Gln															<del>-</del>
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ccg	ggt	gag	cgc	ttt	acg	gac	tcg	cag	ttc	ctg	gtg	cta	atg	aac	cga	598
- 0	J	J0	- 3 -			J		299/		0	J -0		- 70		- 0	<del>-</del>

Pro	Gly	Glu	Arg	Phe	Thr	Asp	Ser	G1n	Phe	Leu	Val	Leu	Met	Asn	Arg	
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Val	Leu	Ala	Leu	Ile	Val	Ala	Gly	Leu	Ser	Cys	Val	Leu	Cys	Lys	Gln	
				165					170					175		
ccc	cgg	cat	ggg	gca	ccc	atg	tac	cgg	tac	tcc	ttt	gcc	agc	ctg	tcc	694
Pro	Arg	His	Gly	Ala	Pro	Met	Tyr	Arg	Tyr	Ser	Phe	Ala	Ser	Leu	Ser .	
			180					185					190			
aat	gtg	ctt	agc	agc	tgg	tgc	caa	tac	gaa	gct	ctt	aag	ttc	gtc	agc	742
Asn	Val		Ser	Ser	Trp	Cys	Gln	Tyr	G1u	Ala	Leu	Lys	Phe	Val	Ser	
		195					200					205				
			cag													790
Phe		Thr	Gln	Val	Leu		Lys	Ala	Ser	Lys		Ile	Pro	Val	Met	
	210					215					220					
										<b>.</b>			<b>.</b>		<b>.</b>	000
			aag													838
225	Mer	GIY	Lys	Leu	230	261	AIR	AIG	Ser	235	GIU	1115	пр	Giu		
220					250					200					240	
ctø	aca	gcc	acc	ctc	atc	tee	att	σσσ	gtc	арс	ato	ttt	ctø	cta	tcc	886
			Thr													000
				245		201		<b>-</b> _,	250				200	255		
				_10												
agc	gga	cca	gag	ccc	CgC	agc	tcc	cca	gcc	acc	a.ca	ctc	tca	ggc	ctc	934
			Glu													
	,		• - "		0			300/		•			<b>-</b>	,		

			260					265					270			
atc	tta	ctg	gca	ggt	tat	att	gct	ttt	gac	agc	ttc	acc	tca	aac	tgg	982
Ile	Leu	Leu	Ala	Gly	Tyr	Ile	Ala	Phe	Asp	Ser	Phe	Thr	Ser	Asn	Trp	
		275					280					285				
cag	gat	gcc	ctg	ttt	gcc	tat	aag	atg	tca	tcg	gtg	cag	atg	atg	ttt	1030
Gln	Asp	Ala	Leu	Phe	Ala	Tyr	Lys	Met	Ser	Ser	Val	Gln	Met	Met	Phe	
	290					295					300					
ggg	gtc	aat	ttc	ttc	tcc	tgc	ctc	ttc	aca	gtg	ggc	tca	ctg	cta	gaa	1078
Gly	Val	Asn	Phe	Phe	Ser	Cys	Leu	Phe	Thr	Val	Gly	Ser	Leu	Leu	Glu	
305					310					315					320	
cag	ggg	gcc	cta	ctg	gag	gga	acc	cgc	ttc	atg	ggg	cga	cac	agt	gag	1126
		Ala														
				325		·			330		•	J		335		
ttt	gct	gcc	cat	gcc	ctg	cta	ctc	tcc	atc	tgc	tcc	gca	tet	ggc	cag	1174
		Ala												_	_	
			340					345		-,-			350	<b>01</b> )	<b>0111</b>	
								0.10								
ctc	tte	atc	ttt	tac	acc	att	aaa	cao	+++	σσσ	act	acc	atc	ttc	200	1222
		Ile														1666
Dou	1110	355	1110	1 7 1	Alla	110		OIII	1110	Oly	nia		141	THE	1111	
		555					360					365				
2+4	n+ -	nt~	200	oto	0.50	25~	~~~	+++	<b></b>	nt n	a++	a++		<b>.</b>		1070
		atg.														1270
Ile	T1~	Ma+	Th∽	1011	A~~	<u> </u>	Λ T ~	Dh a	ΛT~	Tla	I	T	C	C	T	

PCT/JP01/11389

WO 02/053737

375

ctc	tat	ggc	cac	act	gtc	act	gtg	gtg	gga	ggg	ctg	ggg	gtg	gct	gtg	1318
Leu	Tyr	Gly	His	Thr	Val	Thr	Val	Val	Gly	Gly	Leu	Gly	Val	Ala	Val	
385					390					395					400	

gtc ttt gct gcc ctc ctg ctc aga gtc tac gcg cgg ggc cgt cta aag 1366
Val Phe Ala Ala Leu Leu Leu Arg Val Tyr Ala Arg Gly Arg Leu Lys
405 410 415

caa cgg gga aag aag gct gtg cct gtt gag tct cct gtg cag aag gtt 1414 Gln Arg Gly Lys Lys Ala Val Pro Val Glu Ser Pro Val Gln Lys Val 420 425 430

tgagggtgga aagggcctga ggggtgaagt gaaataggac ceteceacea teeeettetg 1474

ctgtaacete tgagggaget ggetgaaagg geaaaatgea ggtgttttet eagtateaca 1534

gaccagetet geageagggg attggggage ceaggaggea geetteeett ttgeettaag 1594

teaceeatet teeagtaage agtttattet gageeeeggg ggtagacagt ceteagtgag 1654

gggttttggg gagtttgggg teaagaagge ataggtaggt teeacagtta etetteeeae 1714

aagtteeett aagtettgee etagetgtee tetgeeacet teeagaetea eteeettet 1774

caaatacetg catttettae eetggtgaga aaageacaag eggtgtagge teeaatgetg 1834

ettteeeagg agggtgaaga tggtgetgtg etgaggaaag gggatgeaga geeetgeeea 1894

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ctgc 2018

⟨210⟩ 87

<211> 235

<212> PRT

<213> Homo sapiens

<400> 87

Met Gly Ile Gly Lys Ser Lys Ile Asn Ser Cys Pro Leu Ser Leu Ser

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Trp Gly Lys Arg His Ser Val Asp Thr Ser Pro Gly Tyr His Glu Ser
20 25 30

Asp Ser Lys Lys Ser Glu Asp Leu Ser Leu Cys Asn Val Ala Glu His
35 40 45

Ser Asn Thr Thr Glu Gly Pro Thr Gly Lys Gln Glu Gly Ala Gln Ser
50 55 60

Val Glu Glu Met Phe Glu Glu Glu Ala Glu Glu Glu Val Phe Leu Lys
65 70 75 80

Phe Val Ile Leu His Ala Glu Asp Asp Thr Asp Glu Ala Leu Arg Val 303/735

85 90 95

Gln Asn Leu Leu Gln Asp Asp Phe Gly Ile Lys Pro Gly Ile Ile Phe 100 105 110

Ala Glu Met Pro Cys Gly Arg Gln His Leu Gln Asn Leu Asp Asp Ala 115 120 125

Val Asn Gly Ser Ala Trp Thr Ile Leu Leu Leu Thr Glu Asn Phe Leu
130 135 140

Arg Asp Thr Trp Cys Asn Phe Gln Phe Tyr Thr Ser Leu Met Asn Ser 145 150 155 160

Val Asn Arg Gln His Lys Tyr Asn Ser Val Ile Pro Met Arg Pro Leu 165 170 175

Asn Asn Pro Leu Pro Arg Glu Arg Thr Pro Phe Ala Leu Gln Thr Ile 180 185 190

Asn Ala Leu Glu Glu Glu Ser Arg Gly Phe Pro Thr Gln Val Glu Arg 195 200 205

Ile Phe Gln Glu Ser Val Tyr Lys Thr Gln Gln Thr Ile Trp Lys Glu 210 215 220

Thr Arg Asn Met Val Gln Arg Gln Phe Ile Ala 225 230 235

<210> 88

<211> 2717

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (111).. (815)

<400> 88

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aaatgctgag aaatacataa agttttcctc ttctgccttg gatatttata atg ggt 116 Met Gly

1

15

atc ggg aag tot aaa ata aat too tgc cot ott tot otc tot tgg ggt 164 Ile Gly Lys Ser Lys Ile Asn Ser Cys Pro Leu Ser Leu Ser Trp Gly 5

10

aaa agg cac agt gtg gat aca agt cca gga tat cat gag tca gat tcc 212 Lys Arg His Ser Val Asp Thr Ser Pro Gly Tyr His Glu Ser Asp Ser 20 25 30

aag aag tot gaa gat ota too tig igt aat git got gag oac ago aat 260 Lys Lys Ser Glu Asp Leu Ser Leu Cys Asn Val Ala Glu His Ser Asn 35 40 45 50

aca	aca	gag	ggg	cca	aca	gga	aag	cag	gag	gga	gct	cag	agc	gtg	gaa	308
Thr	Thr	Glu	Gly	Pro	Thr	Gly	Lys	Gln	Glu	Gly	Ala	Gln	Ser	Val	Glu	
				55					60					65		
gag	atg	ttt	gaa	gaa	gaa	gct	gaa	gaa	gag	gtg	ttc	ctc	aaa	ttt	gtg	356
G1u	Met	Phe	Glu	Glu	Glu	Ala	Glu	Glu	Glu	Val	Phe	Leu	Lys	Phe	Val	
			70					75					80			
ata	ttg	cat	gca	gaa	gat	gac	aca	gat	gaa	gcc	ctc	aga	gtc	cag	aat	404
Ile	Leu	His	Ala	Glu	Asp	Asp	Thr	Asp	G1u	Ala	Leu	Arg	Val	Gln	Asn	
		85					90					95				
ctg	cta	caa	gat	gac	ttt	ggt	atc	aaa	ССС	gga	ata	atc	ttt	gct	gag	452
Leu	Leu	Gln	Asp	Asp	Phe	Gly	Ile	Lys	Pro	Gly	Ile	Ile	Phe	Ala	Glu	
	100					105					110					
atg	cca	tgt	ggc	aga	cag	cat	tta	cag	aat	tta	gat	gat	gct	gta	aat	500
Met	Pro	Cys	Gly	Arg	Gln	His	Leu	G1n	Asn	Leu	Asp	Asp	Ala	Val	Asn	
115					120	•				125					130	
ggg	tct	gca	tgg	aca	atc	tta	tta	ctg	act	gaa	aac	ttt	tta	aga	gat	548
G1y	Ser	Ala	Trp	Thr	Ile	Leu	Leu	Leu	Thr	Glu	Asn	Phe	Leu	Arg	Asp	
				135					140					145		
act	tgg	tgt	aat	ttc	cag	ttc	tat	acg	tcc	cta	atg	aac	tcc	gtt	aac	596
Thr	Trp	Cys	Asn	Phe	Gln	Phe	Tyr	Thr	Ser	Leu	Met	Asn	Ser	Val	Asn	
			150					155					160			
agg	cag	cat	aaa	tac	aac	tct	gtt			atg	cgg	ccc	ctg	aac	aat	644
								306/	735							

Arg Gln His Lys Tyr Asn Ser Val Ile Pro Met Arg Pro Leu Asn Asn 165 170 175

ccc ctt ccc cga gaa agg act ccc ttt gcc ctc caa acc atc aat gcc 692
Pro Leu Pro Arg Glu Arg Thr Pro Phe Ala Leu Gln Thr Ile Asn Ala
180 185 190

tta gag gaa gaa agt cgt gga ttt cct aca caa gta gaa aga att ttt 740 Leu Glu Glu Glu Ser Arg Gly Phe Pro Thr Gln Val Glu Arg Ile Phe 195 200 205 210

cag gag tot gtg tat aag aca caa caa act ata tgg aaa gag aca aga 788

Gln Glu Ser Val Tyr Lys Thr Gln Gln Thr Ile Trp Lys Glu Thr Arg

215 220 225

aat atg gta caa aga caa ttt att gcc tgagatgaaa catataacat 835 Asn Met Val Gln Arg Gln Phe Ile Ala

235

230

ggaaatgttt aaataaaga gagtetteac ettaaagaaa eetatggage acaagaaga 955
taaatteetg caggacagee tataaaattg tggtactttt tgatgttea gtaaacttga 1015
cattgteaga gttteaagga etttette acaatttee tagteatgg atatgaaaaa 1075
ggaattetea ateeatatte ettgtattga acettgaaca aaaacttgta tgacagacat 1135

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gttgaattga tggatctcta aaggcttttg tcctctatga ggatgtgaaa aactagggac 2095 cacaaaaggg aacaagcaaa aaagtttgga ttcgataaag tgatatgtaa tagttgcaga 2155 aggetttata tatgettata atgaaaagat attttttgta tattgacage ataatttatt 2215 tttaatgetg teattacaet taaagteaca ggaaaaaaat atacatgett acteaggett 2275 tcttaaaaat aaatttttat agagatcctt gagtaaagac attttgctta atttcttttt 2335 tettattece eaettgtata teecetacea gtacegggat etgeacacat etttttgeag 2395 ttacctcttc atagccatga accaaaacgt tctatgagga gcatgcaagt aagtcaagcc 2455 tectattetg ttagtaetta ttagaggagg agatggtttt cattgeatag tgacatttte 2515 ttagccttaa cgttctgata gtagcttact actcacttct ctttttcagt tttcataata 2575 agtatteatt tttttgecat aatgetteet gtaaageeaa ttttatatae taataaaaca 2635 tgaactgccc actcttcatg cctgccaaac ttggggcaat tgatgctaaa tggtattttt 2695 aaaataaatg tttttattct tt 2717

<210> 89

<211> 245

<212> PRT

<213> Homo sapiens

<400> 89

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Phe Lys Ser Val Leu Leu Ile Tyr Thr Phe Ile Phe Trp Ile Thr Gly
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Val Ile Leu Leu Ala Val Gly Ile Trp Gly Lys Val Ser Leu Glu Asn 35 40 45

Tyr Phe Ser Leu Leu Asn Glu Lys Ala Thr Asn Val Pro Phe Val Leu 50 55 60

Ile Ala Thr Gly Thr Val Ile Ile Leu Leu Gly Thr Phe Gly Cys Phe
65 70 75 80

Ala Thr Cys Arg Ala Ser Ala Trp Met Leu Lys Leu Tyr Ala Met Phe
85 90 95

Leu Thr Leu Val Phe Leu Val Glu Leu Val Ala Ala Ile Val Gly Phe
100 105 110

Val Phe Arg His Glu Ile Lys Asn Ser Phe Lys Asn Asn Tyr Glu Lys
115 120 125

Ala Leu Lys Gln Tyr Asn Ser Thr Gly Asp Tyr Arg Ser His Ala Val

130 135 140

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Asp Lys Ile Gln Asn Thr Leu His Cys Cys Gly Val Thr Asp Tyr Arg 145 150 155 160

Asp Trp Thr Asp Thr Asn Tyr Tyr Ser Glu Lys Gly Phe Pro Lys Ser 165 170 175

Cys Cys Lys Leu Glu Asp Cys Thr Pro Gln Arg Asp Ala Asp Lys Val 180 185 190

Asn Asn Glu Gly Cys Phe Ile Lys Val Met Thr Ile Ile Glu Ser Glu
195 200 205

Met Gly Val Val Ala Gly Ile Ser Phe Gly Val Ala Cys Phe Gln Leu 210 215 220

Ile Gly Ile Phe Leu Ala Tyr Cys Leu Ser Arg Ala Ile Thr Asn Asn 225 230 235 240

Gln Tyr Glu Ile Val

245

<210> 90

<211> 1793

<212> DNA

<213> Homo sapiens

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<221> CDS

<222> (60).. (794)

<400> 90

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atg gcg tcc ccg tct cgg aga ctg cag act aaa cca gtc att act tgt 107

Met Ala Ser Pro Ser Arg Arg Leu Gln Thr Lys Pro Val Ile Thr Cys

1 5 10 15

ttc aag agc gtt ctg cta atc tac act ttt att ttc tgg atc act ggc 155

Phe Lys Ser Val Leu Leu Ile Tyr Thr Phe Ile Phe Trp Ile Thr Gly
20 25 30

gtt atc ctt ctt gca gtt ggc att tgg ggc aag gtg agc ctg gag aat 203
Val Ile Leu Leu Ala Val Gly Ile Trp Gly Lys Val Ser Leu Glu Asn
35 40 45

tac ttt tct ctt tta aat gag aag gcc acc aat gtc ccc ttc gtg ctc 251

Tyr Phe Ser Leu Leu Asn Glu Lys Ala Thr Asn Val Pro Phe Val Leu

50 55 60

att gct act ggt acc gtc att att ctt ttg ggc acc ttt ggt tgt ttt 299

Ile Ala Thr Gly Thr Val Ile Ile Leu Leu Gly Thr Phe Gly Cys Phe

65 70 75 80

gct acc tgc cga gct tct gca tgg atg cta aaa ctg tat gca atg ttt 347 Ala Thr Cys Arg Ala Ser Ala Trp Met Leu Lys Leu Tyr Ala Met Phe

> 85 90 95 312/735

ctg	act	ctc	gtt	ttt	ttg	gtc	gaa	ctg	gtc	gct	gcc	atc	gta	gga	ttt	395
Leu	Thr	Leu	Val	Phe	Leu	Val	Glu	Leu	Val	Ala	Ala	Ile	Val	Gly	Phe	
			100					105					110			
gtt	ttc	aga	cat	gag	att	aag	aac	agc	ttt	aag	aat	aat	tat	gag	aag	443
Val	Phe	Arg	His	Glu	Ile	Lys	Asn	Ser	Phe	Lys	Asn	Asn	Tyr	Glu	Lys	
		115					120					125				
gct	ttg	aag	cag	tat	aac	tct	aca	gga	gat	tat	aga	agc	cat	gca	gta	491
Ala	Leu	Lys	Gln	Tyr	Asn	Ser	Thr	Gly	Asp	Tyr	Arg	Ser	His	Ala	Val	
	130					135					140					
gac	aag	atc	caa	aat	acg	ttg	cat	tgt	tgt	ggt	gtc	acc	gat	tat	aga	539
Asp	Lys	Ile	G1n	Asn	Thr	Leu	His	Cys	Cys	Gly	Val	Thr	Asp	Tyr	Arg	
145					150		>			155				•	160	
gat	tgg	aca	gat	act	aat	tat	tac	tca	gaa	aaa	gga	ttt	cct	aag	agt	587
Asp	Trp	Thr	Asp	Thr	Asn	Tyr	Tyr	Ser	Glu	Lys	Gly	Phe	Pro	Lys	Ser	
				165					170					175		
tgc	tgt	aaa	ctt	gaa	gat	tgt	act	cca	cag	aga	gat	gca	gac	aaa	gta	635
Cys	Cys	Lys	Leu	Glu	Asp	Cys	Thr	Pro	Gln	Arg	Asp	Ala	Asp	Lys	Val	
			180					185					190		•	
														tca	_	683
Asn	Asn		Gly	Cys	Phe	Ile		Val	Met	Thr	Ile		Glu	Ser	G1u	
		195					200					205				

atg gga gtc gtt gca gga att tcc ttt gga gtt gct tgc ttc caa ctg 731 Met Gly Val Val Ala Gly Ile Ser Phe Gly Val Ala Cys Phe Gln Leu 210 215 220

att gga atc ttt ctc gcc tac tgc ctc tct cgt gcc ata aca aat aac 779

Ile Gly Ile Phe Leu Ala Tyr Cys Leu Ser Arg Ala Ile Thr Asn Asn

225 230 235 240

cag tat gag ata gtg taacccaatg tatctgtggg cctattcctc tctaccttta 834 Gln Tyr Glu Ile Val

245

aggacattta gggtcccccc tgtgaattag aaagttgctt ggctggagaa ctgacaacac 894
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cagagagtca cattgtgtaa tttaatttca gtcagtcaat agatggcatc cctcatcagg 1434
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ttcgtttgtg cctttgatta ataagtataa ctcttataca ataaatactg ctttcctct 1793

<210> 91

<211> 180

<212> PRT

<213> Homo sapiens

<400> 91

Met Ala Ser Thr Ser Tyr Asp Tyr Cys Arg Val Pro Met Glu Asp Gly

1 5 10 15

Asp Lys Arg Cys Lys Leu Leu Cly Ile Gly Ile Leu Val Leu Leu
20 25 30

Ile Ile Val Ile Leu Gly Val Pro Leu Ile Ile Phe Thr Ile Lys Ala 315/735

		35					40					45			
Asn	Ser 50	Glu	Ala	Cys	Arg	Asp 55	Gly	Leu	Arg	Ala	Val 60	Met	Glu	Cys	Arg
Asn 65	Val	Thr	His	Leu	Leu 70	Gln	Gln	Glu	Leu	Thr 75	Glu	Ala	Gln	Lys	Gly 80
Phe	Gln	Asp	Val	G1u 85	Ala	Gln	Ala	Ala	Thr 90	Cys	Asn	His	Thr	Val 95	Met
Ala	Leu	Met	Ala 100	Ser	Leu	Asp	Ala	Glu 105	Lys	Ala	Gln	G1y	Gln 110	Lys	Lys
Val	G1u	Glu 115	Leu	G1u	Gly	Glu	Ile 120	Thr	Thr	Leu	Asn	His 125	Lys	Leu	G1n
Asp	Ala [.] 130	Ser	Ala	Glu	Val	G1u 135	Arg	Leu	Arg	Arġ	Glu 140	Asn	Gln	Val	Leu
Ser 145	Val	Arg	Ile	Ala	Asp 150	Lys	Lys	Tyr	Tyr	Pro 155	Ser	Ser	Gln	Asp	Ser 160
Ser	Ser	Ala	Ala	Ala 165	Pro	G1n	Leu	Leu	Ile 170	Val	Leu	Leu	G1y	Leu 175	Ser

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Ala Leu Leu Gln

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180

<210> 92

<211> 970

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (26).. (565)

<400> 92

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Met Ala Ser Thr Ser Tyr Asp Tyr Cys

1 5

aga gtg ccc atg gaa gac ggg gat aag cgc tgt aag ctt ctg ctg ggg 100
Arg Val Pro Met Glu Asp Gly Asp Lys Arg Cys Lys Leu Leu Gly
10 15 20 25

ata gga att ctg gtg ctc ctg atc atc gtg att ctg ggg gtg ccc ttg 148

Ile Gly Ile Leu Val Leu Leu Ile Ile Val Ile Leu Gly Val Pro Leu

30 35 40

att atc ttc acc atc aag gcc aac agc gag gcc tgc cgg gac ggc ctt 196

Ile Ile Phe Thr Ile Lys Ala Asn Ser Glu Ala Cys Arg Asp Gly Leu

45 50 55

cgg gca gtg atg gag tgt cgc aat gtc acc cat ctc ctg caa caa gag  $\,$  244 Arg Ala Val Met Glu Cys Arg Asn Val Thr His Leu Leu Gln Glu  $\,$  317/735

		60					65					70				
ctg	acc	gag	gcc	cag	aag	ggc	ttt	cag	gat	gtg	gag	gcc	cag	gct	gcc	292
Leu	Thr	Glu	Ala	Gln	Lys	Gly	Phe	Gln	Asp	Val	Glu	Ala	Gln	Ala	Ala	
	75					80					85					
acc	tgc	aac	cac	act	gtg	atg	gcc	cta	atg	gct	tcc	ctg	gat	gca	gag	340
Thr	Cys	Asn	His	Thr	Val	Met	Ala	Leu	Met	Ala	Ser	Leu	Asp	Ala	Glu	
90					95					100					105	
aag	gcc	caa	gga	caa	aag	aaa	gtg	gag	gag	ctt	gag	gga	gag	atc	act	388
Lys	Ala	Gln	Gly	G1n	Lys	Lys	Val	G1u	Glu	Leu	Glu	Gly	Glu	Ile	Thr	
				110					115					120		
aca	tta	aac	cat	aag	ctt	cag	gac	gcg	tct	gca	gag	gtg	gag	cga	ctg	436
Thr	Leu	Asn	His	Lys	Leu	Gln	Asp	Ala	Ser	Ala	Glu	Val	Glu	Arg	Leu	
			125					130					135			
aga	aga	gaa	aac	cag	gtc	tta	agc	gtg	aga	atc	gcg	gac	aag	aag	tac	484
Arg	Arg	G1u	Asn	Gln	Val	Leu	Ser	Val	Arg	Ile	Ala	Asp	Lys	Lys	Tyr	
		140					145					150				
tac	ccc	agc	tcc	cag	gac	tcc	agc	tcc	gct	gcg	gcg	ccc	cag	ctg	ctg	532
Tyr	Pro	Ser	Ser	Gln	Asp	Ser	Ser	Ser	Ala	Ala	Ala	Pro	Gln	Leu	Leu	
	155					160					165					

att gtg ctg ctg ggc ctc agc gct ctg ctg cag tgagatccca ggaagctggc 585

318/735

180

Ile Val Leu Leu Gly Leu Ser Ala Leu Leu Gln

175

170

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<210> 93

<211> 331

<212> PRT

<213> Homo sapiens

<400> 93

Met Asp Ser Glu Lys Lys Arg Phe Thr Glu Glu Ala Thr Lys Tyr Phe

1 5 10 15

Arg Glu Arg Val Ser Pro Val His Leu Gln IIe Leu Leu Thr Asn Asn 20 25 30

Glu Ala Trp Lys Arg Phe Val Thr Ala Ala Glu Leu Pro Arg Asp Glu 319/735

35 40 45

Ala Asp Ala Leu Tyr Glu Ala Leu Lys Lys Leu Arg Thr Tyr Ala Ala
50 55 60

Ile Glu Asp Glu Tyr Val Gln Gln Lys Asp Glu Gln Phe Arg Glu Trp
65 70 75 80

Phe Leu Lys Glu Phe Pro Gln Val Lys Arg Lys Ile Gln Glu Ser Ile 85 90 95

Glu Lys Leu Arg Ala Leu Ala Asn Gly Ile Glu Glu Val His Arg Gly
100 105 110

Cys Thr Ile Ser Asn Val Val Ser Ser Ser Thr Gly Ala Ala Ser Gly
115 120 125

Ile Met Ser Leu Ala Gly Leu Val Leu Ala Pro Phe Thr Ala Gly Thr
130 135 140

Ser Leu Ala Leu Thr Ala Ala Gly Val Gly Leu Gly Ala Ala Ser Ala 145 150 155 160

Val Thr Gly Ile Thr Thr Ser Ile Val Glu His Ser Tyr Thr Ser Ser 165 170 175

Ala Glu Ala Glu Ala Ser Arg Leu Thr Ala Thr Ser Ile Asp Arg Leu 180 185 190

Lys Val Phe Lys Glu Val Met Arg Asp Ile Thr Pro Asn Leu Leu Ser 195 200 205

Leu Leu Asn Asn Tyr Tyr Glu Ala Thr Gln Thr Ile Gly Ser Glu Ile 210 215 220

Arg Ala Ile Arg Gln Ala Arg Ala Arg Leu Pro Val Thr Thr 225 230 235 240

Trp Arg Ile Ser Ala Gly Ser Gly Gly Gln Ala Glu Arg Thr Ile Ala 245 250 255

Gly Thr Thr Arg Ala Val Ser Arg Gly Ala Arg Ile Leu Ser Ala Thr
260 265 270

Thr Ser Gly Ile Phe Leu Ala Leu Asp Val Val Asn Leu Val Tyr Glu 275 280 285

Ser Lys His Leu His Glu Gly Ala Lys Ser Ala Ser Ala Glu Glu Leu 290 295 300

Arg Arg Gln Ala Gln Glu Leu Glu Glu Asn Leu Met Glu Leu Thr Gln 305 310 315 320

Ile Tyr Gln Arg Leu Asn Pro Cys His Thr His
325 330

<210> 94

<211> 2039

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (175).. (1167)

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<400> 94

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tcagtgactg gagageteca aggaaagtet etcagtgace tggetgetgg cace atg 177
Met

1

15

gac tca gaa aag aaa cgc ttt act gaa gag gcc acc aaa tac ttc cgg 225 Asp Ser Glu Lys Lys Arg Phe Thr Glu Glu Ala Thr Lys Tyr Phe Arg

10

gag aga gtc agc cca gtg cat ctg caa atc ctg ctg act aac aat gaa 273 Glu Arg Val Ser Pro Val His Leu Gln Ile Leu Leu Thr Asn Asn Glu

20 25 30

gcc tgg aag aga ttc gtg act gcg gct gaa ttg ccc agg gat gag gca 321 Ala Trp Lys Arg Phe Val Thr Ala Ala Glu Leu Pro Arg Asp Glu Ala

35 40 45

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	. 200

gat	gct	ctc	tac	gaa	gct	ctg	aag	aag	ctt	aga	aca	tat	gca	gct	att	369
Asp	Ala	Leu	Tyr	Glu	Ala	Leu	Lys	Lys	Leu	Arg	Thr	Tyr	Ala	Ala	Ile	
50					55					60					65	
gag	gac	gaa	tat	gtg	cag	cag	aaa	gat	gag	cag	ttt	agg	gaa	tgg	ttt	417
G1u	Asp	G1u	Tyr	Val	Gln	G1n	Lys	Asp	Glu	Gln	Phe	Arg	Glu	Trp	Phe	
				70					75					80		
ttg	aaa	gag	ttt	ccc	caa	gtc	aag	agg	aag	atc	cag	gag	tcc	ata	gaa	465
Leu	Lys	Glu	Phe	P.ro	G1n	Val	Lys	Arg	Lys	Ile	Gln	Glu	Ser	Ile	Glu	
			85					90					95			
aag	ctt	cgt	gcc	ctt	gca	aat	ggt	att	gaa	gag	gtc	cac	aga	ggc	tgc	513
Lys	Leu	Arg	Ala	Leu	Ala	Asn	Gly	Ile	Glu	Glu	Val	His	Arg	Gly	Cys	
		100					105					110				
acc	atc	tcc	aac	gtg	gtg	tcc	agc	tcc	act	ggc	gct	gcc	tct	ggc	atc	561
Thr	Ile	Ser	Asn	Val	Val	Ser	Ser	Ser	Thr	Gly	Ala	Ala	Ser	Gly	Ile	
	115					120					125					
								gca								609
	Ser	Leu	Ala	Gly		Val	Leu	Ala	Pro	Phe	Thr	Ala	Gly	Thr		
130					135					140					145	
								ggg								657
Leu	Ala	Leu	Thr		Ala	Gly	Val	Gly		Gly	Ala	Ala	Ser		Val	
				150					155					160		
act	ggg	atc	acc	acc	agc	atc	gtg	gag 323/		tca	tac	aca	tca	tca	gca	705

Thr Gly Ile Thr Thr Ser Ile Val Glu His Ser Tyr Thr Ser Ser Ala gaa gct gaa gcc agc agg ctg act gca acc agc att gac cga ttg aag Glu Ala Glu Ala Ser Arg Leu Thr Ala Thr Ser Ile Asp Arg Leu Lys gta ttt aag gaa gtt atg cgt gac atc aca ccc aac tta ctt tcc ctt Val Phe Lys Glu Val Met Arg Asp Ile Thr Pro Asn Leu Leu Ser Leu ctt aat aat tat tac gaa gcc aca caa acc att ggg agt gaa atc cgt Leu Asn Asn Tyr Tyr Glu Ala Thr Gln Thr Ile Gly Ser Glu Ile Arg gcc atc agg caa gcc aga gcc agg gcc cga ctc cct gtg acc acc tgg Ala Ile Arg Gln Ala Arg Ala Arg Ala Arg Leu Pro Val Thr Thr Trp cga atc tca gct gga agt ggt ggt caa gca gag aga acg att gca ggc Arg Ile Ser Ala Gly Ser Gly Gly Gln Ala Glu Arg Thr Ile Ala Gly acc acc cgg gca gtg agc aga gga gcc cgg atc ctg agt gcg acc act Thr Thr Arg Ala Val Ser Arg Gly Ala Arg Ile Leu Ser Ala Thr Thr tca ggc atc ttc ctt gca ctg gat gtg gtc aac ctt gta tac gag tca Ser Gly Ile Phe Leu Ala Leu Asp Val Val Asn Leu Val Tyr Glu Ser

275 280 285

aag cac ttg cat gag ggg gca aag tct gca tct gct gag gag ctg agg 1089 Lys His Leu His Glu Gly Ala Lys Ser Ala Ser Ala Glu Glu Leu Arg 290 295 300 305

cgg cag gct cag gag ctg gag gag aat cta atg gag ctc act cag atc 1137

Arg Gln Ala Gln Glu Leu Glu Glu Asn Leu Met Glu Leu Thr Gln Ile

310 315 320

tat cag cgt ctg aat cca tgc cat acc cac tgaccccaga ccagtgcagc 1187
Tyr Gln Arg Leu Asn Pro Cys His Thr His

330

325

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ttccaagaat gaagtctttc cctggtgatg gtcccctgcc ctgtctttcc agcatccact 1667
325/735

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cacctactca cc 2039

<210> 95

<211> 407

<212> PRT

<213> Homo sapiens

<400> 95

Met Glu Leu Leu Glu Glu Asp Leu Thr Cys Pro Ile Cys Cys Ser Leu

1 5 10 15

Phe Asp Asp Pro Arg Val Leu Pro Cys Ser His Asn Phe Cys Lys Lys
20 25 30

Cys Leu Glu Gly Ile Leu Glu Gly Ser Val Arg Asn Ser Leu Trp Arg 326/735

		35					40					45			
Pro	Ala 50	Pro	Phe	Lys	Cys	Pro 55	Thr	Cys	Arg	Lys	G1u 60	Thr	Ser	Ala	Thr
Gly 65	Ile	Asn	Ser	Leu	Gln 70	Val	Asn	Tyr	Ser	Leu 75	Lys	Gly	Ile	Val	Glu 80
Lys	Tyr	Asn	Lys	Ile 85	Lys	Ile	Ser	Pro	Lys 90	Met	Pro	Val	Cys	Lys 95	Gly
His	Leu	Gly	Gln 100	Pro	Leu	Asn	Ile	Phe 105	Cys	Leu	Thr	Asp	Met 110	G1n	Leu
Ile	Cys	Gly 115	Ile	Cys	Ala	Thr	Arg 120	Gly	Glu	His	Thr	Lys 125	His	Val	Phe
Cys	Ser 130	Ile	Glu	Asp	Ala	Tyr 135	Ala	Gln	Glu	Arg	Asp 140	Ala	Phe	G1u	Ser
Leu 145	Phe	G1n	Ser	Phe	Glu 150	Thr	Trp	Arg	Arg	Gly 155	Asp	Ala	Leu	Ser	Arg 160
Leu	Asp	Thr	Leu	Glu 165	Thr	Ser	Lys	Arg	Lys 170	Ser	Leu	Gln	Leu	Leu 175	Thr
Lys	Asp	Ser	Asp	Lys	Val	Lys	Glu	Phe	Phe	G1u	Lys	Leu	Gln	His	Thr

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185

190

180

Leu	Asp	Gln	Lys	Lys	Asn	Glu	Ile	Leu	Ser	Asp	Phe	Glu	Thr	Met	Lys
		195					200					205			
Leu	Ala	Val	Met	Gln	Ala	Tyr	Asp	Pro	Glu	Ile	Asn	Lys	Leu	Asn	Thr
	210					215					220				
Ile	Leu	G1n	Glu	Gln	Arg	Met	Ala	Phe	Asn	Ile	Ala	G1u	Ala	Phe	Lys
225					230					235					240
Asp	Val	Ser	Glu	Pro	Ile	Val	Phe	Leu	Gln	Gln	Met	Gln	Glu	Phe	Arg
				245					250					255	
Glu	Lys	Ile		Val	Ile	Lys	Glu		Pro	Leu	Pro	Pro		Asn	Leu
			260					265					270		
Pro	Ala		Pro	Leu	Met	Lys		Phe	Asp	Thr	Ser		Trp	Glu	Asp
		275					280					285			
Ile		Leu	Val	Asp	Val		Lys	Leu	Ser	Leu		Gln	Asp	Thr	Gly
	290					295					300				
Thr	Phe	Ile	Ser	Lys	Ile	Pro	Trp	Ser	Phe	Tyr	Lys	Leu	Phe	Leu	Leu
305					310					315					320
Ile	Leu	Leu	Leu	Gly	Leu	Val	Ile	Val	Phe	Gly	Pro	Thr	Met	Phe	Leu
				325					330					335	
G1u	Trp	Ser		Phe	Asp	Asp	Leu		Thr	Trp	Lys	Gly		Leu	Ser
			340					345					350		

Asn Phe Ser Ser Tyr Leu Thr Lys Thr Ala Asp Phe Ile Glu Gln Ser 355 360 365

Val Phe Tyr Trp Glu Gln Val Thr Asp Gly Phe Phe Ile Phe Asn Glu 370 375 380

Arg Phe Lys Asn Phe Thr Leu Val Val Leu Asn Asn Val Ala Glu Phe 385 390 395 400

Val Cys Lys Tyr Lys Leu Leu 405

<210> 96

<211> 1409

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (181).. (1401)

<400> 96

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ttcccactag ccggagtagc ctctagttcg ttagtcaaaa cgtgaaaaaa aaagacctgc 120

tttgccctgg gaaatagtaa ccctgccaaa tacatcagct tgtaggagac agaggatgtg 180 329/735

atg	gag	ctg	ctt	gaa	gaa	gat	ctc	aca	tgc	cct	att	tgt	tgt	agt	ctg	228
Met	Glu	Leu	Leu	Glu	G1u	Asp	Leu	Thr	Cys	Pro	Ile	Cys	Cys	Ser	Leu	
1				5					10					15		
ttt	gat	gat	cca	cgg	gtt	ttg	cct	tgc	tcc	cac	aac	ttc	tgc	aaa	aaa	276
Phe	Asp	Asp	Pro	Arg	Val	Leu	Pro	Cys	Ser	His	Asn	Phe	Cys	Lys	Lys	
			20					25					30			
tgc	tta	gaa	ggt	atc	tta	gaa	ggg	agt	gtg	cgg	aat	tcc	ttg	tgg	aga	324
Cys	Leu	Glu	Gly	Ile	Leu	Glu	Gly	Ser	Val	Arg	Asn	Ser	Leu	Trp	Arg	
		35					40					45				
cca	gct	cca	ttc	aag	tgt	cct	aca	tgc	cgt	aag	gaa	act	tca	gct	act	372
Pro		Pro	Phe	Lys	Cys	Pro	Thr	Cys	Arg	Lys	Glu	Thr	Ser	Ala	Thr	
	50					55					60					
														gtg		420
	Ile	Asn	Ser	Leu		Val	Asn	Tyr	Ser		Lys	Gly	Ile	Val	Glu	
65					70					75					80	
	_												_	aaa		468
_ys	Tyr	Asn	Lys		Lys	Ile	Ser	Pro	-	Met	Pro	Val	Cys	Lys	Gly	
				85					90					95		
													_	cag	_	516
lis	Leu	Gly		Pro	Leu	Asn	He		Cys	Leu	Thr	Asp		Gln	Leu	
			100					105					110			

att	tgt	ggg	atc	tgt	gct	act	cgt	ggg	gag	cac	acc	aaa	cat	gtc	ttc	564
Ile	Cys	Gly	Ile	Cys	Ala	Thr	Arg	Gly	Glu	His	Thr	Lys	His	Val	Phe	
		115					120					125				
										-						
tgt	tct	att	gaa	gat	gcc	tat	gct	cag	gaa	agg	gat	gcc	ttt	gag	tcc	612
Cys	Ser	Ile	Glu	Asp	Ala	Tyr	Ala	Gln	Glu	Arg	Asp	Ala	Phe	Glu	Ser	
	130					135					140					
ctc	ttc	cag	agc	ttt	gag	acc	tgg	cgt	cgg	gga	gat	gct	ctt	tct	cgc	660
Leu	Phe	Gln	Ser	Phe	Glu	Thr	Trp	Arg	Arg	Gly	Asp	Ala	Leu	Ser	Arg	
145					150					155					160	
ttg	gat	acc	ttg	gaa	act	agt	aag	agg	aaa	tcc	cta	cag	tta	ctg	act	708
Leu	Asp	Thr	Leu		Thr	Ser	Lys	Arg	Lys	Ser	Leu	G1n	Leu	Leu	Thr	
				165					170					175		
	gat															756
Lys	Asp	Ser		Lys	Val	Lys	Glu		Phe	G1u	Lys	Leu		His	Thr	
			180					185					190			
	gat															804
Leu	Asp		Lys	Lys	Asn	Glu		Leu	Ser	Asp	Phe		Thr	Met	Lys	
		195					200					205				
																050
	gct	_	_		_		_								•	852
Leu	Ala	val	Met	GIN	Ala		Asp	Pro	GIU	116		Lys	Leu	Asn	Thr	
	210					215					220					
<b>.</b>	++~	<b>.</b>				a+-		+++	000	a++	~c+			<b></b> .		000
atc	ttg	cag	gag	caa	cgg	atg	gcc	331/		att	gct	gag	gct	ttc	aaa	900

Ile Leu Gln Glu Gln Arg Met Ala Phe Asn Ile Ala Glu Ala Phe Lys gat gtg tca gaa ccc att gta ttt ctg caa cag atg cag gag ttt aga Asp Val Ser Glu Pro Ile Val Phe Leu Gln Gln Met Gln Glu Phe Arg gag aaa atc aaa gta atc aag gaa act cct tta cct ccc tct aat ttg Glu Lys Ile Lys Val Ile Lys Glu Thr Pro Leu Pro Pro Ser Asn Leu cct gca agc cct tta atg aag aac ttt gat acc agt cag tgg gaa gac Pro Ala Ser Pro Leu Met Lys Asn Phe Asp Thr Ser Gln Trp Glu Asp ata aaa cta gtc gat gtg gat aaa ctt tct ttg cct caa gac act ggc Ile Lys Leu Val Asp Val Asp Lys Leu Ser Leu Pro Gln Asp Thr Gly aca ttc att agc aag att ccc tgg agc ttt tat aag tta ttt ttg cta Thr Phe Ile Ser Lys Ile Pro Trp Ser Phe Tyr Lys Leu Phe Leu Leu atc ctt ctg ctt ggc ctt gtc att gtc ttt ggt cct acc atg ttc cta Ile Leu Leu Cly Leu Val Ile Val Phe Gly Pro Thr Met Phe Leu gaa tgg tca tta ttt gat gac ctg gca act tgg aaa ggc tgt ctt tca Glu Trp Ser Leu Phe Asp Asp Leu Ala Thr Trp Lys Gly Cys Leu Ser 332/735

340 345 350

aac ttc agt tcc tat ctg act aaa aca gcc gat ttc ata gaa caa tca 1284

Asn Phe Ser Ser Tyr Leu Thr Lys Thr Ala Asp Phe Ile Glu Gln Ser

355 360 365

gtt ttt tac tgg gaa cag gtg aca gat ggg ttt ttc att ttc aat gaa 1332 Val Phe Tyr Trp Glu Gln Val Thr Asp Gly Phe Phe Ile Phe Asn Glu 370 375 380

aga ttc aag aat ttt act ttg gtg gta ctg aac aat gtg gca gaa ttt 1380 Arg Phe Lys Asn Phe Thr Leu Val Val Leu Asn Asn Val Ala Glu Phe 385 390 395 400

gtg tgc aaa tat aaa cta tta taaaatcg 1409 Val Cys Lys Tyr Lys Leu Leu

⟨210⟩ 97

<211> 465

<212> PRT

<213> Homo sapiens

405

<400> 97

Met Ala Ser Thr Thr Ser Thr Lys Lys Met Met Glu Glu Ala Thr Cys

1 5 10 15

Ser Ile Cys Leu Ser Leu Met Thr Asn Pro Val Ser Ile Asn Cys Gly 333/735

WO 02/05373	7		PCT/JP01/11389	
	20	<b>25</b> .	30	

His Ser Tyr Cys His Leu Cys Ile Thr Asp Phe Phe Lys Asn Pro Ser

35 40 45

Gln Lys Gln Leu Arg Gln Glu Thr Phe Cys Cys Pro Gln Cys Arg Ala
50 55 60

Pro Phe His Met Asp Ser Leu Arg Pro Asn Lys Gln Leu Gly Ser Leu 65 70 75 80

Ile Glu Ala Leu Lys Glu Thr Asp Gln Glu Met Ser Cys Glu Glu His

85 90 95

Gly Glu Gln Phe His Leu Phe Cys Glu Asp Glu Gly Gln Leu Ile Cys 100 105 110

Trp Arg Cys Glu Arg Ala Pro Gln His Lys Gly His Thr Thr Ala Leu 115 120 125

Val Glu Asp Val Cys Gln Gly Tyr Lys Glu Lys Leu Gln Glu Ala Val 130 135 140

Thr Lys Leu Lys Gln Leu Glu Asp Arg Cys Thr Glu Gln Lys Leu Ser 145 150 155 160

Thr Ala Met Arg Ile Thr Lys Trp Lys Glu Lys Val Gln Ile Gln Arg 165 170 175

Gln	Lys	Ile	Arg	Ser	Asp	Phe	Lys	Asn	Leu	Gln	Cys	Phe	Leu	His	Glu
			180					185					190		
01	01	T	C	Т	T	Т	A	1	C1	T	C1	C1	C1	C1	T1
GIU	GIU		Ser	ıyr	Leu	irp		Leu	GIU	Lys	GIU		GIN	GIN	Inr
		195					200					205			
Len	Ser	Aro	Leu	Aro	Asn	Tvr	Glu	Ala	G1v	11ع. آ	G1 v	l.eu	I.ve	Ser	Asn
Dou	210	6	Dou	6	пор	215	010		01)	Dou	220	Dou	2,0	501	11011
						210					220				
Glu	Leu	Lvs	Ser	His	Ile	Leu	Glu	Leu	Glu	Glu	Lvs	Cvs	Gln	Gl v	Ser
225		<b>-,</b> -			230					235	_,_	-,-	<b>7</b>	,	240
220					200					200					210
Ala	G1n	Lvs	Leu	Leu	Gln	Asn	Val	Asn	Asp	Thr	Leu	Ser	Arg	Ser	Trp
		_,_		245					250					255	
Ala	Val	Lys	Leu	Glu	Thr	Ser	G1u	Ala	Val	Ser	Leu	G1u	Leu	His	Thr
			260					265					270		
Met	Cys	Asn	Val	Ser	Lys	Leu	Tyr	Phe	Asp	Val	Lys	Lys	Met	Leu	Arg
		275					280					285			·
Ser	His	G1n	Val	Ser	Val	Thr	Leu	Asp	Pro	Asp	Thr	Ala	His	His	Glu

290 295 300

Leu Ile Leu Ser Glu Asp Arg Gln Val Thr Arg Gly Tyr Thr Gln 305 310 315 320

Glu Asn Gln Asp Thr Ser Ser Arg Arg Phe Thr Ala Phe Pro Cys Val
325
335/735

Leu Gly Cys Glu Gly Phe Thr Ser Gly Arg Arg Tyr Phe Glu Val Asp Val Gly Glu Gly Thr Gly Trp Asp Leu Gly Val Cys Met Glu Asn Val Gln Arg Gly Thr Gly Met Lys Gln Glu Pro Gln Ser Gly Phe Trp Thr Leu Arg Leu Cys Lys Lys Gly Tyr Val Ala Leu Thr Ser Pro Pro Thr Ser Leu His Leu His Glu Gln Pro Leu Leu Val Gly Ile Phe Leu Asp Tyr Glu Ala Gly Val Val Ser Phe Tyr Asn Gly Asn Thr Gly Cys His Ile Phe Thr Phe Pro Lys Ala Ser Phe Ser Asp Thr Leu Arg Pro Tyr Phe Gln Val Tyr Gln Tyr Ser Pro Leu Phe Leu Pro Pro Gly Asp

⟨210⟩ 98

<211> 1940

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (477).: (1871)

<400> 98

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caccaaatct cagaagattc agaacttaga tgagtggggc ccaggacagg aaccctggag 120
ccttggaagg aggggagccc catctcccca gaagagcagt gaccccagca gagaggggcc 180
tggtgtatca ctggaggaaa tagcctgcca aggaatacac gtcttcagaa gaagttctgt 240
gtggcttcaa gagactgatc aaattgtgag aggaaaacag cctacccggt cctctttct 300
tcaatacaaa atgagataat aggggttgga aggaaaacct tcaagaccta tggaagtcag 360
ttgcagccag ctcatcacat agaggtgcag gtgaggtgta ttttcatcac ggtggaaaat 420
tctggctgct tcatctccat ctctagagcc aatattggag cttttcaata aaagct atg 479
Met

1

gcc tca acc acc agc acc aag aag atg atg gag gaa gcc acc tgc tcc 527 337/735

Ala	Ser	Thr	Thr	Ser	Thr	Lys	Lys	Met	Met	G1u	G1u	Ala	Thr	Cys	Ser	
			5					10					15			
atc	tgc	ctg	agc	ctg	atg	acg	aac	cca	gta	agc	atc	aac	tgt	gga	cac	575
Ile	Cys	Leu	Ser	Leu	Met	Thr	Asn	Pro	Val	Ser	Ile	Asn	Cys	Gly	His	
		20					25					30				
agc	tac	tgc	cac	ttg	tgt	ata	aca	gac	ttc	ttt	aaa	aac	cca	agc	caa	623
Ser	Tyr	Cys	His	Leu	Cys	Ile	Thr	Asp	Phe	Phe	Lys	Asn	Pro	Ser	Gln	
	35					40					45					
aag	caa	ctg	agg	cag	gag	aca	ttc	tgc	tgt	ccc	cag	tgt	cgg	gct	cca	671
Lys	Gln	Leu	Arg	Gln	Glu	Thr	Phe	Cys	Cys	Pro	Gln	Cys	Arg	Ala	Pro	
50					55					60					65	
ttt	cat	atg	gat	agc	ctc	cga	ccc	aac	aag	cag	ctg	gga	agc	ctc	att	719
Phe	His	Met	Asp	Ser	Leu	Arg	Pro	Asn		G1n	Leu	Gly	Ser	Leu	Ile	
				70					75					80	•	
														cac		767
Glu	Ala	Leu		Glu	Thr	Asp	Gln		Met	Ser	Cys	Glu		His	Gly	
			85					90					95			
														tgc		815
Glu	Gln		His	Leu	Phe	Cys		Asp	Glu	Gly	Gln		Ile	Cys	Trp	
		100					105					110				
														ctt		863
Arg	Cys	Glu	Arg	Ala	Pro	Gln	His	Lys 338/		His	Thr	Thr	Ala	Leu	Val	
								,								

115 120 125

gaa gac gta tgc cag ggc tac aag gaa aag ctc cag gaa gct gtg aca 911 Glu Asp Val Cys Gln Gly Tyr Lys Glu Lys Leu Gln Glu Ala Val Thr 130 135 140 145

aaa ctg aag caa ctt gaa gac aga tgt acg gag cag aag ctg tcc aca 959
Lys Leu Lys Gln Leu Glu Asp Arg Cys Thr Glu Gln Lys Leu Ser Thr
150 155 160

gca atg cga ata act aaa tgg aaa gag aag gta cag att cag aga caa 1007 Ala Met Arg Ile Thr Lys Trp Lys Glu Lys Val Gln Ile Gln Arg Gln 165 170 175

aaa atc cgg tct gac ttt aag aat ctc cag tgt ttc cta cat gag gaa 1055
Lys Ile Arg Ser Asp Phe Lys Asn Leu Gln Cys Phe Leu His Glu Glu
180 185 190

gag aag tot tat oto tgg agg otg gag aaa gaa gaa caa cag act otg 1103 Glu Lys Ser Tyr Leu Trp Arg Leu Glu Lys Glu Glu Gln Gln Thr Leu 195 200 205

agt aga ctg agg gac tat gag gct ggt ctg ggg ctg aag agc aat gaa 1151 Ser Arg Leu Arg Asp Tyr Glu Ala Gly Leu Gly Leu Lys Ser Asn Glu 210 215 220 225

ctc aag agc cac atc ctg gaa ctg gag gaa aaa tgt cag ggc tca gcc 1199
Leu Lys Ser His Ile Leu Glu Leu Glu Glu Lys Cys Gln Gly Ser Ala
230 235 240
339/735

cag	aaa	ttg	ctg	cag	aat	gtg	aat	gac	act	ttg	agc	agg	agt	tgg	gct	1247
Gln	Lys	Leu	Leu	G1n	Asn	Val	Asn	Asp	Thr	Leu	Ser	Arg	Ser	Trp	Ala	
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gtg	aag	ctg	gaa	aca	tca	gag	gct	gtc	tcc	ttg	gaa	ctt	cat	act	atg	1295
Val	Lys	Leu	Glu	Thr	Ser	Glu	Ala	Val	Ser	Leu	Glu	Leu	His	Thr	Met	
		260					265					270				
tgc	aat	gtt	tcc	aag	ctt	tac	ttc	gat	gtg	aag	aaa	atg	tta	agg	agt	1343
Cys	Asn	Val	Ser	Lys	Leu	Tyr	Phe	Asp	Val	Lys	Lys	Met	Leu	Arg	Ser	
	275		•			280					285					
										aca						1391
	Gln	Val	Ser	Val		Leu	Asp	Pro	Asp	Thr	Ala	His	His	Glu		
290					295					300					305	
												,				1400
										cgt						1439
IIe	Leu	Ser	Glu		Arg	Arg	GIn	vai		Arg	ста	lyr	Inr		Glu	
				310					315					320		
aa+	000	an o	000	+ 0 +	+00	0.55	000	+++	ant	<b>300</b>	++0	000	+ ~+	a+ 0	++ <i>a</i>	1487
										gcc						1401
VOII	OIII	лор	325	261	261	ντα	ΛIΕ	330	1111	MIG	THE	110	335	vai	Leu	
			320					300					555			
ggt.	tgt	gaa	aac	ttc	acc	tca	gga	aga	cgt	tac	ttt	gaa	g t.g	gat	øtt	1535
										Tyr		_	-	_	_	
,	-,-	340	,				345	6	6	-,-		350				

ggc	gaa	gga	acc	gga	tgg	gat	tta	gga	gtt	tgt	atg	gaa	aat	gtg	cag	1583
Gly	Glu	Gly	Thr	Gly	Trp	Asp	Leu	Gly	Val	Cys	Met	Glu	Asn	Val	Gln	
	355					360					365					
agg	ggc	act	ggc	atg	aag	caa	gag	cct	cag	tct	gga	ttc	tgg	acc	ctc	1631
Arg	G1y	Thr	Gly	Met	Lys	G1n	G1u	Pro	G1n	Ser	Gly	Phe	Trp	Thr	Leu	
370					375					380					385	
agg	ctg	tgc	aaa	aag	aaa	ggc	tat	gta	gca	ctt	act	tct	ccc	cca	act	1679
Arg	Leu	Cys	Lys	Lys	Lys	Gly	Tyr	Val	Ala	Leu	Thr	Ser	Pro	Pro	Thr	
				390					395					400		
tcc	ctt	cat	ctg	cat	gag	cag	ссс	ctg	ctt	gtg	gga	att	ttt	ctg	gac	1727
Ser	Leu	His	Leu	His	Glu	Gln	Pro	Leu	Leu	Val	G1y	Ile	Phe	Leu	Asp	
			405					410					415			
															•	
tat	gag	gcc	gga	gtt	gta	tcc	ttt	tat	aac	ggg	aat	act	ggc	tgc	cac	1775
Tyr	G1u	Ala	Gly	Val	Val	Ser	Phe	Tyr	Asn	Gly	Asn	Thr	Gly	Cys	His	
		420					425					430				
atc	ttt	act	ttc	ccg	aag	gct	tcc	ttc	tct	gat	act	ctc	cgg	ссс	tat	1823
Ile	Phe	Thr	Phe	Pro	Lys	Ala	Ser	Phe	Ser	Asp	Thr	Leu	Arg	Pro	Tyr	
	435					440					445					
ttc	cag	gtt	tat	caa	tat	tct	cct	ttg	ttt	ctg	cct	ссс	cca	ggt	gac	1871
Phe	G1n	Val	Tyr	G1n	Tyr	Ser	Pro	Leu	Phe	Leu	Pro	Pro	Pro	Gly	Asp	
450					455					460					465	

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taagggcag 1940

<210> 99

<211> 465

<212> PRT

<213> Homo sapiens

<400> 99

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1 5 10 15

Ser Ile Cys Leu Ser Leu Met Thr Asn Pro Val Ser Ile Asn Cys Gly
20 25 30

His Ser Tyr Cys His Leu Cys Ile Thr Asp Phe Phe Lys Asn Pro Ser
35 40 45

Gln Lys Gln Leu Arg Gln Glu Thr Phe Cys Cys Pro Gln Cys Arg Ala
50 55 60

Pro Phe His Met Asp Ser Leu Arg Pro Asn Lys Gln Leu Gly Ser Leu 65 70 75 80

Ile Glu Ala Leu Lys Glu Thr Asp Gln Glu Met Ser Cys Glu Glu His

85 90 95

Gly Glu Gln Phe His Leu Phe Cys Glu Asp Glu Gly Gln Leu Ile Cys 342/735

WO 02/053737	PCT/JP01/11389

Trp Arg Cys Glu Arg Ala Pro Gln His Lys Gly His Thr Thr Ala Leu Val Glu Asp Val Cys Gln Gly Tyr Lys Glu Lys Leu Gln Lys Ala Val Thr Lys Leu Lys Gln Leu Glu Asp Arg Cys Thr Glu Gln Lys Leu Ser Thr Ala Met Arg Ile Thr Lys Trp Lys Glu Lys Val Gln Ile Gln Arg Gln Lys Ile Arg Ser Asp Phe Lys Asn Leu Gln Cys Phe Leu His Glu Glu Glu Lys Ser Tyr Leu Trp Arg Leu Glu Lys Glu Glu Gln Gln Thr 

Leu Ser Arg Leu Arg Asp Tyr Glu Ala Gly Leu Gly Leu Lys Ser Asn 210 215 220

Glu Leu Lys Ser His Ile Leu Glu Leu Glu Glu Lys Cys Gln Gly Ser 225 230 235 240

Ala Gln Lys Leu Leu Gln Asn Val Asn Asp Thr Leu Ser Arg Ser Trp

245 250 255

Ala Val Lys Leu Glu Thr Ser Glu Ala Val Ser Leu Glu Leu His Thr Met Cys Asn Val Ser Lys Leu Tyr Phe Asp Val Lys Lys Met Leu Arg Ser His Gln Val Ser Val Thr Leu Asp Pro Asp Thr Ala His His Glu Leu Ile Leu Ser Glu Asp Arg Gln Val Thr Arg Gly Tyr Thr Gln Glu Asn Gln Asp Thr Ser Ser Arg Arg Phe Thr Ala Phe Pro Cys Val Leu Gly Cys Glu Gly Phe Thr Ser Gly Arg Arg Tyr Phe Glu Val Asp Val Gly Glu Gly Thr Gly Trp Asp Leu Gly Val Cys Met Glu Asn Val Gln Arg Gly Thr Gly Met Lys Gln Glu Pro Gln Ser Gly Phe Trp Thr Leu Arg Leu Cys Lys Lys Gly Tyr Val Ala Leu Thr Ser Pro Pro

Thr Ser Leu His Leu His Glu Gln Pro Leu Leu Val Gly Ile Phe Leu
405
410
344/735

Asp Tyr Glu Ala Gly Val Val Ser Phe Tyr Asn Gly Asn Thr Gly Cys
420 425 430

His Ile Phe Thr Phe Pro Lys Ala Ser Phe Ser Asp Thr Leu Arg Pro
435
440
445

Tyr Phe Gln Val Tyr Gln Tyr Ser Pro Leu Phe Leu Pro Pro Pro Gly
450 455 460

Asp

465

<210> 100

<211> 1940

<212> DNA

<213> Homo sapiens

⟨220⟩

<221> CDS

<222> (477).. (1871)

<400> 100

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ccttggaagg aggggagccc catctcccca gaagagcagt gaccccagca gagaggggcc 180 345/735

240	ttctgt	gaag	gaa	ttca	gtc	acac	gaata	a ag	tgcca	agcc	aa t	agga	ctgg	tca	tgta	tgg
300	ttttct	cctc	ggt	accc	ccta	acag	gaaaa	gag	gtgag	aatt	tc a	ctga	gaga	caa	gctt	gtg
360	agtcag	tggaa	cta	agac	tca	acct	gaaaa	ag	ttgga	gggg	at a	gata	atga	aaa	ataca	tcaa
420	gaaaat	ggtgį	cac	tcate	ttt	tgta	gaggi	gt	tgcag	gagg	at a	tcac	ctca [.]	cag	cago	ttge
479	ct atg	aaago	ata	ttca	ctt	ggag	tattį	aa ·	gagco	tcta	at c	ctcc	tcat	gct	ggcti	tctį
	Met															
	1															
527	tcc	tgc	acc	gcc	gaa	gag	atg	atg	aag	aag	acc	agc	acc	acc	tca	gcc
	Ser	Cys	Thr	Ala	Glu	Glu	Met	Met	Lys	Lys	Thr	Ser	Thr	Thr	Ser	Ala
			15					10					5			
575		gga	+ a+	990	ato	age	πta	cca	220	30 a	atα	cta	200	cta	tac	atc
010																
	nis	Gly	Cys		116	Set	vaı	110		1111	Mec	Leu	get		Cys	TIE
				30					25					20		
623	caa	agc	cca	aac	aaa	ttt	ttc	gac	aca	ata	tgt	ttg	cac	tgc	tac	agc
	G1n	Ser	Pro	Asn	Lys	Phe	Phe	Asp	Thr	Ile	Cys	Leu	His	Cys	Tyr	Ser
					45					40					35	
671	cca	gct	cgg	tgt	cag	ссс	tgt	tgc	ttc	aca	gag	cag	agg	ctg	caa	aag
	Pro	Ala	Arg	Cys	Gln	Pro	Cys	Cys	Phe	Thr	Glu	Gln	Arg	Leu	Gln	Lys
	65					60					55					50

ttt cat atg gat agc ctc cga ccc aac aag cag ctg gga agc ctc att 719

Phe	His	Met	Asp	Ser	Leu	Arg	Pro	Asn	Lys	Gln	Leu	Gly	Ser	Leu	Ile	
				70					75					80		
gaa	gcc	ctc	aaa	gag	acg	gat	caa	gaa	atg	tca	tgt	gag	gaa	cac	gga	767
Glu	Ala	Leu	Lys	Glu	Thr	Asp	Gln	Glu	Met	Ser	Cys	Glu	Glu	His	Gly	
			85					90					95			
gag	cag	ttc	cac	ctg	ttc	tgc	gaa	gac	gag	ggg	cag	ctc	atc	tgc	tgg	815
Glu	G1n	Phe	His	Leu	Phe	Cys	Glu	Asp	G1u	Gly	Gln	Leu	Ile	Cys	Trp	
		100					105					110				
cgc	tgt	gag	cgg	gca	cca	cag	cac	aaa	ggg	cac	acc	aca	gct	ctt	gtt	863
Arg	Cys	G1u	Arg	A1a	Pro	G1n	His	Lys	Gly	His	Thr	Thr	Ala	Leu	Val	
	115					120					125					
																•
gaa	gac	gta	tgc	cag	ggc	tac	aag	gaa	aag	ctc	cag	aaa	gct	gtg	aca	911
Glu	qzA	Val	Cys	Gln	Gly	Tyr	Lys	Glu	Lys	Leu	Gln	Lys	Ala	Val	Thr	
130					135					140					145	
aaa	ctg	aag	caa	ctt	gaa	gac	aga	tgt	acg	gag	cag	aag	ctg	tcc	aca	959
Lys	Leu	Lys	G1n	Leu	Glu	Asp	Arg	Cys	Thr	G1u	G1n	Lys	Leu	Ser	Thr	
				150					155					160		
gca	atg	cga	ata	act	aaa	tgg	aaa	gag	aag	gta	cag	att	cag	aga	caa	1007
Ala	Met	Arg	Ile	Thr	Lys	Trp	Lys	G1u	Lys	Val	G1n	Ile	Gln	Arg	Gln	
			165					170					175			
aaa	atc	cgg	tct	gac	ttt	aag	aat			tgt	ttc	cta	cat	gag	gaa	1055
								347/	735							

Lys Ile Arg Ser Asp Phe Lys Asn Leu Gln Cys Phe Leu His Glu Glu gag aag tot tat oto tgg agg otg gag aaa gaa gaa caa cag act otg Glu Lys Ser Tyr Leu Trp Arg Leu Glu Lys Glu Glu Gln Gln Thr Leu agt aga ctg agg gac tat gag gct ggt ctg ggg ctg aag agc aat gaa Ser Arg Leu Arg Asp Tyr Glu Ala Gly Leu Gly Leu Lys Ser Asn Glu ctc aag agc cac atc ctg gaa ctg gag gaa aaa tgt cag ggc tca gcc Leu Lys Ser His Ile Leu Glu Leu Glu Glu Lys Cys Gln Gly Ser Ala cag aaa ttg ctg cag aat gtg aat gac act ttg agc agg agt tgg gct Gln Lys Leu Leu Gln Asn Val Asn Asp Thr Leu Ser Arg Ser Trp Ala gtg aag ctg gaa aca tca gag gct gtc tcc ttg gaa ctt cat act atg Val Lys Leu Glu Thr Ser Glu Ala Val Ser Leu Glu Leu His Thr Met tgc aat gtt tcc aag ctt tac ttc gat gtg aag aaa atg tta agg agt Cys Asn Val Ser Lys Leu Tyr Phe Asp Val Lys Lys Met Leu Arg Ser cat caa gtt agt gtg act ctg gat cca gat aca gct cat cac gaa cta His Gln Val Ser Val Thr Leu Asp Pro Asp Thr Ala His His Glu Leu 348/735

att ctc tct gag gat cgg aga caa gtg act cgt gga tac acc cag gag Ile Leu Ser Glu Asp Arg Arg Gln Val Thr Arg Gly Tyr Thr Gln Glu aat cag gac aca tot too agg aga ttt act goo tto coo tgt gto ttg Asn Gln Asp Thr Ser Ser Arg Arg Phe Thr Ala Phe Pro Cys Val Leu ggt tgt gaa ggc ttc acc tca gga aga cgt tac ttt gaa gtg gat gtt Gly Cys Glu Gly Phe Thr Ser Gly Arg Arg Tyr Phe Glu Val Asp Val ggc gaa gga acc gga tgg gat tta gga gtt tgt atg gaa aat gtg cag Gly Glu Gly Thr Gly Trp Asp Leu Gly Val Cys Met Glu Asn Val Gln agg ggc act ggc atg aag caa gag cct cag tct gga ttc tgg acc ctc Arg Gly Thr Gly Met Lys Gln Glu Pro Gln Ser Gly Phe Trp Thr Leu agg ctg tgc aaa aag aaa ggc tat gta gca ctt act tct ccc cca act Arg Leu Cys Lys Lys Gly Tyr Val Ala Leu Thr Ser Pro Pro Thr tcc ctt cat ctg cat gag cag ccc ctg ctt gtg gga att ttt ctg gac Ser Leu His Leu His Glu Gln Pro Leu Leu Val Gly Ile Phe Leu Asp 349/735

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tat gag gcc gga gtt gta tcc ttt tat aac ggg aat act ggc tgc cac 1775

Tyr Glu Ala Gly Val Val Ser Phe Tyr Asn Gly Asn Thr Gly Cys His

420 425 430

atc ttt act ttc ccg aag gct tcc ttc tct gat act ctc cgg ccc tat 1823

Ile Phe Thr Phe Pro Lys Ala Ser Phe Ser Asp Thr Leu Arg Pro Tyr

435

440

445

ttc cag gtt tat caa tat tct cct ttg ttt ctg cct ccc cca ggt gac 1871
Phe Gln Val Tyr Gln Tyr Ser Pro Leu Phe Leu Pro Pro Pro Gly Asp
450 455 460 465

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taagggcag 1940

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<211> 685

<212> PRT

<213> Homo sapiens

<400> 101

Met Glu Leu Leu Arg Thr Ile Thr Tyr Gln Pro Ala Ala Ser Thr Lys

1 5 10 15

Met Cys Glu Gln Ala Leu Gly Lys Gly Cys Gly Ala Asp Ser Lys Lys
20 25 30

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Lys Arg Pro Pro Gln Pro Pro Glu Glu Ser Gln Pro Pro Gln Ser Gln Ala Gln Val Pro Pro Ala Ala Pro His His His His His Ser His Ser Gly Pro Glu Ile Ser Arg Ile Ile Val Asp Pro Thr Thr Gly Lys Arg Tyr Cys Arg Gly Lys Val Leu Gly Lys Gly Gly Phe Ala Lys Cys Tyr Glu Met Thr Asp Leu Thr Asn Asn Lys Val Tyr Ala Ala Lys Ile Ile Pro His Ser Arg Val Ala Lys Pro His Gln Arg Glu Lys Ile Asp Lys Glu Ile Glu Leu His Arg Ile Leu His His Lys His Val Val Gln Phe Tyr His Tyr Phe Glu Asp Lys Glu Asn Ile Tyr Ile Leu Leu Glu Tyr Cys Ser Arg Arg Ser Met Ala His Ile Leu Lys Ala Arg Lys Val 

Leu Thr Glu Pro Glu Val Arg Tyr Tyr Leu Arg Gln Ile Val Ser Gly

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Leu Lys Tyr Leu His Glu Gln Glu Ile Leu His Arg Asp Leu Lys Leu Gly Asn Phe Phe Ile Asn Glu Ala Met Glu Leu Lys Val Gly Asp Phe Gly Leu Ala Ala Arg Leu Glu Pro Leu Glu His Arg Arg Thr Ile Cys Gly Thr Pro Asn Tyr Leu Ser Pro Glu Val Leu Asn Lys Gln Gly His Gly Cys Glu Ser Asp Ile Trp Ala Leu Gly Cys Val Met Tyr Thr .260 Met Leu Leu Gly Arg Pro Pro Phe Glu Thr Thr Asn Leu Lys Glu Thr Tyr Arg Cys Ile Arg Glu Ala Arg Tyr Thr Met Pro Ser Ser Leu Leu Ala Pro Ala Lys His Leu Ile Ala Ser Met Leu Ser Lys Asn Pro Glu

Asp Arg Pro Ser Leu Asp Asp Ile Ile Arg His Asp Phe Phe Leu Gln
325 330 335

VO 02/053737	PCT/JP01/11389

Gly	Phe	Thr	Pro 340	Asp	Arg	Leu	Ser	Ser 345	Ser	Cys	Cys	His	Thr 350	Val	Pro
Asp	Phe	His 355	Leu	Ser	Ser	Pro	Ala 360	Lys	Asn	Phe	Phe	Lys 365	Lys	Ala	Ala
Ala	Ala 370	Leu	Phe	Gly	Gly	Lys 375	Lys	Asp	Lys	Ala	Arg 380	Tyr	Ile	Asp	Thr
His 385	Asn	Arg	Val	Ser	Lys 390	Glu	Asp	Glu	Asp	Ile 395	Tyr	Lys	Leu	Arg	His 400
Asp	Leu	Lys	Lys	Thr 405	Ser	Ile	Thr	Gln	Gln 410	Pro	Ser	Lys	His	Arg 415	Thr
Asp	G1u	Glu	Leu 420	G1n	Pro	Pro	Thr	Thr 425		Val	Ala	Arg	Ser 430	Gly	Thr
Pro	Ala	Val 435	Glu	Asn	Lys	G1n	G1n 440	Ile	Gly	Asp	Ala	Ile 445	Arg	Met	Ile
Val	Arg 450	Gly	Thr	Leu	Gly	Ser 455	Cys	Ser	Ser	Ser	Ser 460	Glu	Cys	Leu	G1u
Asp 465	Ser	Thr	Met	G1y	Ser 470	Val	Ala	Asp	Thr	Val 475	Ala	Arg	Val	Leu	Arg 480
Gly	Cys	Leu	Glu	Asn	Met	Pro	Glu	Ala	Asp	Cys	Ile	Pro	Lys	Glu	Gln

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Leu	Ser	Thr	Ser 500	Phe	Gln	Trp	Val	Thr 505	Lys	Trp	Val	Asp	Tyr 510	Ser	Asn
Lys	Tyr	Gly 515	Phe	Gly	Tyr	Gln	Leu 520	Ser	Asp	His	Thr	Val 525	Gly	Val	Leu
Phe	Asn 530	Asn	Gly	Ala	His	<b>Met</b> 535	Ser	Leu	Leu	Pro	Asp 540	Lys	Lys	Thr	Val
His 545	Tyr	Tyr	Ala	Glu	Leu 550	Gly	Gln	Cys	Ser	Val 555	Phe	Pro	Ala	Thr	Asp 560
Ala	Pro	Glu	Gln	Phe 565	Ile	Ser	Gln	Val	Thr 570	Val	Leu	Lys	Tyr	Phe 575	Ser
His	Tyr	Met	Glu 580	Glu	Asn	Leu	Met	Asp 585	Gly	Gly	Asp	Leu	Pro 590	Ser	Val
Thr	Asp	Ile 595	Arg	Arg	Pro	Arg	Leu 600	Tyr	Leu	Leu	Ğ1n	Trp 605	Leu	Lys	Ser
Asp		Ala	Leu	Met	Met			Asn	Asp	Gly	Thr 620		Gln	Val	Asn
	610 Tyr	His	Asp	His		615 Lys	Ile	Ile	Ile		•	Gln	Asn	Glu	
625 Tyr	Leu	Leu	Thr	Tyr	630 Ile	Asn	G1u	Asp	Arg	635 Ile	Ser	Thr	Thr	Phe	640 Arg

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645 650 655

Leu Thr Thr Leu Leu Met Ser Gly Cys Ser Ser Glu Leu Lys Asn Arg
660 665 670

Met Glu Tyr Ala Leu Asn Met Leu Leu Gln Arg Cys Asn 675 680 685

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<211> 2783

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<220>

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<400> 102

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cggccggctc ggacgtgtga ccgcgcctag ggggtggcag cgggcagtgc ggggcggcaa 120

ggcgacc atg gag ctt ttg cgg act atc acc tac cag cca gcc gcc agc 169
Met Glu Leu Arg Thr Ile Thr Tyr Gln Pro Ala Ala Ser

10

acc aaa atg tgc gag cag gcg ctg ggc aag ggt tgc gga gca gac tcg 217
Thr Lys Met Cys Glu Gln Ala Leu Gly Lys Gly Cys Gly Ala Asp Ser
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				20					25					30	
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Lys	Lys	Arg	Pro	Pro	Gln	Pro	Pro	Glu	Glu	Ser	Gln	Pro	Pro	Gln	
			35					40					45		
cag	gcg	caa	gtg	ccc	ccg	gcg	gcc	cct	cac	cac	cat	cac	cac	cat	313
Gln	Ala	Gln	Val	Pro	Pro	Ala	Ala	Pro	His	His	His	His	His	His	
		50					55					60			
cac	tcg	ggg	ccg	gag	atc	tcg	cgg	att	atc	gtc	gac	ccc	acg	act	361
His	Ser	Gly	Pro	Glu	Ile	Ser	Arg	Ile	Ile	Val	Asp	Pro	Thr	Thr	
	65					70					75				
aag	cgc	tac	tgc	cgg	ggc	aaa	gtg	ctg	gga	aag	ggt	ggc	ttt	gca	409
															•
		-	-							90					
tgt	tac	gag	atg	aca	gat	ttg	aca	aat	aac	aaa	gtc	tac	gcc	gca	457
-,-	-,-	<b>V</b>													
				100											
att	att	cct	cac	age	202	σta	get	ลลล	cct	cat	caa	agg	ฮลล	ลลฮ	505
116	116	110		Der	ΛIE	741	nia		110	1113	OIN	ME		БуЗ	
			110					120					125		
					_44			_++	_44				+	-+-	552
															553
Asp	Lys		TTE	Glu	Leu	H1S		TIE	Leu	nıs	HIS		HIS	vai	
		130						/735				140			
	Lys cag Gln cac His aag Lys 80 tgt Cys att Ile	cag gcg Gln Ala  cac tcg His Ser 65  aag cgc Lys Arg 80  tgt tac Cys Tyr  att att Ile Ile	Cag gcg caa Gln Ala Gln 50  Cac tcg ggg His Ser Gly 65  aag cgc tac Lys Arg Tyr 80  tgt tac gag Cys Tyr Glu  att att cct Ile Ile Pro	Lys Lys Arg Pro 35  Cag gcg caa gtg Gln Ala Gln Val 50  Cac tcg ggg ccg His Ser Gly Pro 65  aag cgc tac tgc Lys Arg Tyr Cys 80  tgt tac gag atg Cys Tyr Glu Met  att att cct cac Ile Ile Pro His 115  gac aaa gaa ata Asp Lys Glu Ile	aag       aag       ccg       ccg         Lys       Lys       Arg       Pro       Pro         cag       gcg       caa       gtg       ccc         Gln       Ala       Gln       Val       Pro         50       sgg       ccg       gag         cac       tcg       ggg       ccg       gag         His       Ser       Gly       Pro       Glu         aag       cgc       tac       tgc       cgg         Lys       Arg       Tyr       Cys       Arg         80       tac       gag       atg       aca         Cys       Tyr       Glu       Met       Thr         100       tat       ccc       agc         Ile       Pro       His       Ser         115       tac       gag       ata       gag         Asp       Lys       Glu       Ile       Glu	aag       aag       ccg       ccg       cag         Lys       Lys       Arg       Pro       Pro       Gln         cag       gcg       caa       gtg       ccc       ccg         Gln       Ala       Gln       Val       Pro       Pro         cac       tcg       ggg       ccg       gag       atc         His       Ser       Gly       Pro       Glu       Ile         aag       cgc       tac       tgc       cgg       ggc         Lys       Arg       Tyr       Cys       Arg       Gly         80       Tyr       Cys       Arg       gat         tgt       tac       gag       atg       aca       gat         tgt       tac       gag       atg       aca       gat         tgt       tac       gac       atg       aca       gat         tgt       tac       agc       atg       atg       aca       gat         tgt       tac       cac       agc       aga       atg       at	aag       aag       cag       ccg       cag       ccc         Lys       Arg       Pro       Pro       Gln       Pro         cag       gcg       cag       gtg       ccc       ccg       gcg         Gln       Ala       Gln       Val       Pro       Pro       Ala         50       scg       gag       atc       tcg       tcg       Hro       Pro       Ala       tcg       aaa       tcg       aaa       tcg       aaa       tag       aaa       tcg       aaa       aaa       ttg       tcg       gac       aaa       ttg       tcg       tcg       aaa       ttg       tcg       tcg       aaa       ttg       tcg       tcg       aaa       ttg       tcg       tcg       aaa       ttg       tcg       tc	aag       aag       ccg       ccg       cag       ccc       ccc         Lys       Lys       Arg       Pro       Pro       Gln       Pro       Pro         cag       gcg       cag       gcc       ccg       gcg       gcc         Gln       Ala       Gln       Val       Pro       Pro       Ala       Ala         cac       tcg       ggg       ccg       gag       atc       tcg       cgg         cac       tcg       ggg       ccg       gag       atc       tcg       cgg         daa       cgc       tac       tgc       cgg       ggc       aaa       gtg         lys       Arg       Tyr       Cys       Arg       Gly       Lys       Val         ag       tac       gad       aca       gat       ttg       aca         tgt       tac       gad       aca       gat       ttg       aca         tgt       tac       aga       aga       gta       gct       aca       gct         tgt       tac       cac       agc       aga       gta       gct       aca       gct       aca       aga       gt	aag aag cag cag cag cag cag cag cag cag	aag aag cag cag cag cag cag cag aag aag	aag aag aag cag cag cag cag cag cag cag	aag       aag       cag       ccg       cag       cac       ccc       gag       gaa       tcg       cag         Lys       Lys       Arg       Pro       Pro       Gln       Pro       Pro       Glu       Glu       Glu       Ser       Gln         cag       gcg       caa       gtg       ccc       ccg       gcg       gcc       cac       cat         Gln       Ala       Gln       Val       Pro       Pro       Ala       Ala       Pro       His       H	aag aag cag cag cag cag cag cag cag cag	aag aag cgg ccg ccg ccg ccg ccg ccg ccc ccc	aag aag cag cag cag cag cag cag cag cag

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gtg	cag	ttt	tac	cac	tac	ttc	gag	gac	aaa	gaa	aac	att	tac	att	ctc	601
Val	Gln	Phe	Tyr	His	Tyr	Phe	Glu	Asp	Lys	Glu	Asn	Ile	Tyr	Ile	Leu	
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Leu	Glu	Tyr	Cys	Ser	Arg	Arg	Ser	Met	Ala	His	Ile	Leu	Lys	Ala	Arg	
	160					165					170					
aag	gtg	ttg	aca	gag	cca	gaa	gtt	cga	tac	tac	ctc	agg	cag	att	gtg	697
Lys	Val	Leu	Thr	Glu	Pro	G1u	Val	Arg	Tyr	Tyr	Leu	Arg	Gln	Ile	Val	
175					180					185					190	
tct	gga	ctg	aaa	tac	ctt	cat	gaa	caa	gaa	atc	ttg	cac	aga	gat	ctc	745
Ser	Gly	Leu	Lys	Tyr	Leu	His	Glu	Gln	Glu	Ile	Leu	His	Arg	Asp	Leu	
				195					200					205		
aaa	cta	ggg	aac	ttt	ttt	att	aat	gaa	gcc	atg	gaa	cta	aaa	gtt	ggg	793
Lys	Leu	Gly	Asn	Phe	Phe	I1e	Asn	Glu	Ala	Met	Glu	Leu	Lys	Val	Gly	
			210					215					220			
gac	ttc	ggt	ctg	gca	gcc	agg	cta	gaa	ссс	ttg	gaa	cac	aga	agg	aga	841
Asp	Phe	G1y	Leu	Ala	Ala	Arg	Leu	Glu	Pro	Leu	G1u	His	Arg	Arg	Arg	
		225					230					235				
acg	ata	tgt	ggt	acc	cca	aat	tat	ctc	tct	cct	gaa	gtc	ctc	aac	aaa	889
Thr	Ile	Cys	Gly	Thr	Pro	Asn	Tyr	Leu	Ser	Pro	Glu	Va1	Leu	Asn	Lys	
	240					245					250				•	

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Gln	G1 y	His	Gly	Cys	Glu	Ser	Asp	Ile	Trp	Ala	Leu	Gly	Cys	Val	Met	
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tat	aca	atg	tta	cta	ggg	agg	ccc	cca	ttt	gaa	act	aca	aat	ctc	aaa	985
Tyr	Thr	Met	Leu	Leu	Gly	Arg	Pro	Pro	Phe	Glu	Thr	Thr	Asn	Leu	Lys	
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gaa	act	tat	agg	tgc	ata	agg	gaa	gca	agg	tat	aca	atg	ccg	tcc	tca	1033
G1u	Thr	Tyr	Arg	Cys	Ile	Arg	Glu	Ala	Arg	Tyr	Thr	Met	Pro	Ser	Ser	
			290					295					300			
	•															
ttg	ctg	gct	cct	gcc	aag	cac	tta	att	gct	agt	atg	ttg	tcc	aaa	aac	1081
Leu	Leu	Ala	Pro	Ala	Lys	His	Leu	Ile	Ala	Ser	Met	Leu	Ser	Lys	Asn	
		305					310					315				
cca	gag	gat	cgt	ccc	agt	ttg	gat	gac	atc	att	cga	cat	gac	ttt	ttt	1129
Pro	Glu	Asp	Arg	Pro	Ser	Leu	Asp	Asp	Ile	Ile	Arg	His	Asp	Phe	Phe	
	320					325					330					
ttg	cag	ggc	ttc	act	ccg	gac	aga	ctg	tct	tct	agc	tgt	tgt	cat	aca	1177
Leu	G1n	Gly	Phe	Thr	Pro	Asp	Arg	Leu	Ser	Ser	Ser	Cys	Cys	His	Thr	
335					340					345					350	
gtt	cca	gat	ttc	cac	tta	tca	agc	cca	gct	aag	aat	ttc	ttt	aag	aaa	1225
Val	Pro	Asp	Phe	His	Leu	Ser	Ser	Pro	Ala	Lys	Asn	Phe	Phe	Lys	Lys	
				355					360					365		
gca	gct	gct	gct	ctt	ttt	ggt	ggc	aaa		gac	aaa	gca	aga	tat	att	1273
								358/	133							

Ala	Ala	Ala	Ala	Leu	Phe	G1y	Gly	Lys	Lys	Asp	Lys	Ala	Arg	Tyr	Ile	
			370					375					380			
gac	aca	cat	aat	aga	gtg	tct	aaa	gaa	gat	gaa	gac	atc	tac	aag	ctt	1323
Asp	Thr	His	Asn	Arg	Val	Ser	Lys	Glu	Asp	Glu	Asp	Ile	Tyr	Lys	Leu	
		385					390					395			•	
agg	cat	gat	ttg	aaa	aag	act	tca	ata	act	cag	caa	ccc	agc	aaa	cac	1369
Arg	His	Asp	Leu	Lys	Lys	Thr	Ser	Ile	Thr	Gln	Gln	Pro	Ser	Lys	His	
	400					405					410					
agg	aca	gat	gag	gag	ctc	cag	cca	cct	acc	acc	aca	gtt	gcc	agg	tct	1417
Arg	Thr	Asp	Glu	Glu	Leu	Gln	Pro	Pro	Thr	Thr	Thr	Val	Ala	Arg	Ser	
415					420					425					430	
gga	aca	ссс	gca	gta	gaa	aac	aag	cag	cag	att	ggg	gat	gct	att	cgg	1465
Gly	Thr	Pro	Ala	Val	Glu	Asn	Lys	G1n	G1n	Ile	Gly	Asp	Ala	Ile	Arg	
				435					440					445		
atg	ata	gtc	aga	ggg	act	ctt	ggc	agc	tgt	agc	agc	agc	agt	gaa	tgc	1513
Met	Ile	Val	Arg	Gly	Thr	Leu	Gly	Ser	Cys	Ser	Ser	Ser	Ser	Glu	Cys	
			450					455					460			
ctt	gaa	gac	agt	acc	atg	gga	agt	gtt	gca	gac	aca	gtg	gca	agg	gtt	1561
Leu	G1u	Asp	Ser	Thr	Met	Gly	Ser	Va1	Ala	Asp	Thr	Val	Ala	Arg	Val	
		465					470					475				
ctt	cgg	gga	tgt	ctg	gaa	aac	atg	ccg	gaa	gct	gat	tgc	att	ccc	aaa	1609
Leu	Arg	Gly	Cys	Leu	Glu	Asn	Met	Pro	G1u	Ala	Asp	Cys	Ile	Pro	Lys	
								359/	735							

WO 02/053737

480

485

490

gag cag ctg agc aca tca ttt cag tgg gtc acc aaa tgg gtt gat tac 1657

gag cag ctg agc aca tca ttt cag tgg gtc acc aaa tgg gtt gat tac 1657
Glu Gln Leu Ser Thr Ser Phe Gln Trp Val Thr Lys Trp Val Asp Tyr
495 500 505 510

tct aac aaa tat ggc ttt ggg tac cag ctc tca gac cac acc gtc ggt 1705 Ser Asn Lys Tyr Gly Phe Gly Tyr Gln Leu Ser Asp His Thr Val Gly 515 520 525

gtc ctt ttc aac aat ggt gct cac atg agc ctc ctt cca gac aaa aaa 1753
Val Leu Phe Asn Asn Gly Ala His Met Ser Leu Leu Pro Asp Lys Lys
530 535 540

aca gtt cac tat tac gca gag ctt ggc caa tgc tca gtt ttc cca gca 1801 Thr Val His Tyr Tyr Ala Glu Leu Gly Gln Cys Ser Val Phe Pro Ala 545 550 555

aca gat gct cct gag caa ttt att agt caa gtg acg gtg ctg aaa tac 1849

Thr Asp Ala Pro Glu Gln Phe Ile Ser Gln Val Thr Val Leu Lys Tyr

560 565 570

ttt tct cat tac atg gag gag aac ctc atg gat ggt gga gat ctg cct 1897
Phe Ser His Tyr Met Glu Glu Asn Leu Met Asp Gly Gly Asp Leu Pro
575 580 585 590

agt gtt act gat att cga aga cct cgg ctc tac ctc ctt cag tgg cta 1945

Ser Val Thr Asp Ile Arg Arg Pro Arg Leu Tyr Leu Leu Gln Trp Leu

595 600 605

360/735

aaa	tct	gat	aag	gcc	cta	atg	atg	ctc	ttt	aat	gat	ggc	acc	ttt	cag	1993
Lys	Ser	Asp	Lys	Ala	Leu	Met	Met	Leu	Phe	Asn	Asp	Gly	Thr	Phe	Gln	
			610					615					620			
gtg	aat	ttc	tac	cat	gat	cat	aca	aaa	atc	atc	atc	tgt	agc	caa	aat	2041
Val	Asn	Phe	Tyr	His	Asp	His	Thr	Lys	Ile	Ile	Ile	Cys	Ser	Gln	Asn	
		625					630					635				
gaa	gaa	tac	ctt	ctc	acc	tac	atc	aat	gag	gat	agg	ata	tct	aca	act	2089
Glu	Glu	Tyr	Leu	Leu	Thr	Tyr	Ile	Asn	Glu	Asp	Arg	Ile	Ser	Thr	Thr	
	640					645					650					
ttc	agg	ctg	aca	act	ctg	ctg	atg	tct	ggc	tgt	tca	tca	gaa	tta	aaa	2137
Phe	Arg	Leu	Thr	Thr	Leu	Leu	Met	Ser	Gly	Cys	Ser	Ser	Glu	Leu	Lys	
655					660					665					670	
aat	cga	atg	gaa	tat	gcc	ctg	aac	atg	ctc	tta	caa	aga	tgt	aac		2182
Asn	Arg	Met	G1u	Tyr	Ala	Leu	Asn	Met	Leu	Leu	G1n	Arg	Cys	Asn		
				675					680					685		
tgaa	agac	tt t	tcga	atgg	ga co	ctat	ggga	cto	ctct	ttt	ccac	tgtg	ag a	atcta	caggg	2242
aacc	caaa	ag a	atga	tcta	ag ag	gtate	ttga	aga	agat	gga	cate	tggt	gg 1	acga	aaaca	2302
atto	ccct	gt g	gcct	gcte	gg ac	tggg	tgga	acc	agaa	cag	gcta	aggo	at a	acagt	tcttg	2362
actt	tgga	ica a	tcca	agag	gt ga	acca	gaat	gca	gttt	tcc	ttga	gata	icc t	gttt	taaaa	2422

ggtttttcag acaattitge agaaaggtge attgattett aaattetee tgttgagage 2482
attteageea gaggaettig gaactgtgaa tataetteet gaaggggagg gagaagggag 2542
gaageteeca tgttgttaa aggetgtaat tggageaget tttggetges taactgtgaa 2602
ctatggeeat atataattit tttteattaa ttttgaaga taettgtgge tggaaaagtg 2662
catteettgt taataaactt tttatttatt acageecaaa gageagtatt tattaeaa 2722
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<210> 103

<211> 161

<212> PRT

<213> Homo sapiens

<400> 103

Met Ser Val Pro Gly Pro Tyr Gln Ala Ala Thr Gly Pro Ser Ser Ala

1 5 10 15

Pro Ser Ala Pro Pro Ser Tyr Glu Glu Thr Val Ala Val Asn Ser Tyr
20 25 30

Tyr Pro Thr Pro Pro Ala Pro Met Pro Gly Pro Thr Thr Gly Leu Val
35
40
45
362/735

Thr Gly Pro Asp Gly Lys Gly Met Asn Pro Pro Ser Tyr Tyr Thr Gln
50 55 60

Pro Ala Pro Ile Pro Asn Asn Pro Ile Thr Val Gln Thr Val Tyr
65 70 75 80

Val Gln His Pro Ile Thr Phe Leu Asp Arg Pro Ile Gln Met Cys Cys 85 90 95

Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn Ala Gly
100 105 110

Ala Leu Thr Trp Leu Ser Cys Gly Ser Leu Cys Leu Leu Gly Cys Ile 115 120 125

Ala Gly Cys Cys Phe Ile Pro Phe Cys Val Asp Ala Leu Gln Asp Val 130 135 140

Asp His Tyr Cys Pro Asn Cys Arg Ala Leu Leu Gly Thr Tyr Lys Arg 145 150 155 160

Leu

<210> 104

<211> 1589

<212> DNA

363/735

<213> Homo sapiens

<220>

<221> CDS

<222> (70).. (552)

<400> 104

cetttteteg gggcgcccga aggccagete agaceteccg getegacagg eggcgeggge 60

ggcggtaaa atg tcg gtt cca gga cct tac cag gcg gcc act ggg cct tcc 111

Met Ser Val Pro Gly Pro Tyr Gln Ala Ala Thr Gly Pro Ser

1 5 10

tca gca cca tcc gca cct cca tcc tat gaa gag aca gtg gct gtt aac 159
Ser Ala Pro Ser Ala Pro Pro Ser Tyr Glu Glu Thr Val Ala Val Asn
15 20 25 30

agt tat tac ccc aca cct cca gct ccc atg cct ggg cca act acg ggg 207

Ser Tyr Tyr Pro Thr Pro Pro Ala Pro Met Pro Gly Pro Thr Thr Gly

35 40 45

ctt gtg acg ggg cct gat ggg aag ggc atg aat cct cct tcg tat tat 255
Leu Val Thr Gly Pro Asp Gly Lys Gly Met Asn Pro Pro Ser Tyr Tyr
50 55 60

acc cag cca gcg ccc atc ccc aat aac aat cca att acc gtg cag acg 303

Thr Gln Pro Ala Pro Ile Pro Asn Asn Pro Ile Thr Val Gln Thr
65 70 75

364/735

Val Tyr Val Gln His Pro Ile Thr Phe Leu Asp Arg Pro Ile Gln Met 80 85 90  tgt tgt cct tcc tgc aac aag atg atc gtg agt cag ctg tcc tat aac Cys Cys Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn 95 100 105 110  gcc ggt gct ctg acc tgg ctg tcc tgc ggg agc ctg tgc ctg ctg ggg Ala Gly Ala Leu Thr Trp Leu Ser Cys Gly Ser Leu Cys Leu Leu Gly	399 447
tgt tgt cct tcc tgc aac aag atg atc gtg agt cag ctg tcc tat aac Cys Cys Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn 95 100 105 110 gcc ggt gct ctg acc tgg ctg tcc tgc ggg agc ctg tgc ctg ctg ggg	
Cys Cys Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn 95 100 105 110 gcc ggt gct ctg acc tgg ctg tcc tgc ggg agc ctg tgc ctg ctg ggg	
Cys Cys Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn 95 100 105 110 gcc ggt gct ctg acc tgg ctg tcc tgc ggg agc ctg tgc ctg ctg ggg	
95 100 105 110  gcc ggt gct ctg acc tgg ctg tcc tgc ggg agc ctg tgc ctg ctg ggg	447
gcc ggt gct ctg acc tgg ctg tcc tgc ggg agc ctg tgc ctg ctg ggg	447
	447
	447
Ala Gly Ala Leu Thr Trp Leu Ser Cvs Gly Ser Leu Cys Leu Leu Gly	
115 120 125	
tgc ata gcg ggc tgc tgc ttc atc ccc ttc tgc gtg gat gcc ctg cag	495
Cys Ile Ala Gly Cys Cys Phe Ile Pro Phe Cys Val Asp Ala Leu Gln	
130 135 140	
gac gtg gac cat tac tgt ccc aac tgc aga gct ctc ctg ggc acc tac	543
Asp Val Asp His Tyr Cys Pro Asn Cys Arg Ala Leu Leu Gly Thr Tyr	
145 150 155	
aag cgt ttg taggactcag ccagacgtgg agggagccgg gtgccgcagg	592
Lys Arg Leu	
160	
aagteettte caceteteat ecagetteae geetggtgga ggttetgeee tggtggtete	652
acctctccag ggggcccacc ttcatgtctt cttttggggg gaatacgtcg caaaactaac	712
aaatctccaa accccagaaa ttgctgcttg gagtcgtgca taggacttgc aaagacattc 365/735	772

cccttgagtg tcagttccac ggtttcctgc ctccctgaga ccctgagtcc tgccatctaa 832 ctgtgatcat tgccctatcc gaatatcttc ctgtgatctg ccatcagtgg ctcttttttc 892 ctgcttccat gggcctttct ggtggcagtc tcaaactgag aagccacagt tgccttattt 952 ttgaggctgt tctgcccaga gctcggctga accagccttt agtgcctacc attatcttat 1012 tgagattctg taactgcaga cttcattagc acacagattc actttaattt cttaattttt 1132 tttttaaata caaggaggg gctattaaca cccagtacag acatatccac aaggtcgtaa 1192 atgcatgcta gaaaaatagg gctggatctt atcactgccc tgtctcccct tgtttctctg 1252 tgccagatct tcagtgcccc tttccataca gggatttttt tctcatagag taattatatg 1312 aacagttttt atgacctcct tttggtctga aatactttcg aacagaattt ctttttttta 1372 aaaaaaaaaa gagatggggt cttactatgt tgcccaggct ggtgtcgaac tcctgggctc 1432 aagcgatcct tetgeettgg cetecegaag tgetgggatt geaggcataa getaceatge 1492 tgggcctgaa cataatttca agaggaggat ttataaaaacc attttctgta atcaaatgat 1552 tggtgtcatt ttcccatttg ccaatgtagt ctcactt 1589

<210> 105

<211> 161

<212> PRT

<213> Homo sapiens

<400> 105

Met Ser Val Pro Gly Pro Tyr Gln Ala Ala Thr Gly Pro Ser Ser Ala

1 5 10 15

Pro Ser Ala Pro Pro Ser Tyr Glu Glu Thr Val Ala Val Asn Ser Tyr
20 25 30

Tyr Pro Thr Pro Pro Ala Pro Met Pro Gly Pro Thr Thr Gly Leu Val
35 40 45

Thr Gly Pro Asp Gly Lys Gly Met Asn Pro Pro Ser Tyr Tyr Thr Gln
50 55 60

Pro Ala Pro Ile Pro Asn Asn Pro Ile Thr Val Gln Thr Val Tyr
65 70 75 80

Val Gln His Pro Ile Thr Phe Leu Asp Arg Pro Val Gln Met Cys Cys
85 90 95

Pro Ser Cys Asn Lys Met Ile Val Ser Gln Leu Ser Tyr Asn Ala Gly
100 105 110

Ala Leu Thr Trp Leu Ser Cys Gly Ser Leu Cys Leu Leu Gly Cys Ile 367/735

115 120 125

Ala Gly Cys Cys Phe Ile Pro Phe Cys Val Asp Ala Leu Gln Asp Val 130 135 140

Asp His Tyr Cys Pro Asn Cys Arg Ala Leu Leu Gly Thr Tyr Lys Arg 145 150 155 160

Leu

<210> 106

<211> 1589

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (70).. (552)

1

<400> 106

cettteteg gggegeeega aggeeagete agaeeteeeg getegaeagg eggegegge 60

ggcggtaaa atg tcg gtt cca gga cct tac cag gcg gcc act ggg cct tcc 111

Met Ser Val Pro Gly Pro Tyr Gln Ala Ala Thr Gly Pro Ser

10

5

tca gca cca tcc gca cct cca tcc tat gaa gag aca gtg gct gtt aac 159
368/735

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,, ,	

Ser	Ala	Pro	Ser	Ala	Pro	Pro	Ser	Tyr	Glu	Glu	Thr	Val	Ala	Val	Asn	
15					20					25					30	
o.=+	+-+	+00			+		~a+		o+~	+	~~~		00+		~~~	207
															ggg	207
261	1 9 1	1 9 1	110	35	110	110	VIG	110	40	110	GIY	110	1111	45	Gly	
				00					10					40		
ctt	gtg	acg	ggg	cct	gat	ggg	aag	ggc	atg	aat	cct	cct	tcg	tat	tat	255
Leu	Val	Thr	Gly	Pro	Asp	Gly	Lys	Gly	Met	Asn	Pro	Pro	Ser	Tyr	Tyr	
			50					55					60			
acc	cag	cca	gcg	ccc	atc	ccc	aat	aac	aat	cca	att	acc	gtg	cag	acg	303
Thr	Gln	Pro	Ala	Pro	Ile	Pro	Asn	Asn	Asn	Pro	Ile	Thr	Val	Gln	Thr	
		65					70					75				
	4					_4_			44_			4	_4_		_ #	0.51
						atc										351
Val	80	Val	GIII	1115	110	Ile 85	1111	rne	Leu	лър	90 A1 g	110	Val	GIII	Mec	
						00										
tgt	tgt	cct	tcc	tgc	aac	aag	atg	atc	gtg	agt	cag	ctg	tcc	tat	aac	399
Cys	Cys	Pro	Ser	Cys	Asn	Lys	Met	Ile	Val	Ser	G1n	Leu	Ser	Tyr	Asn	
95					100					105					110	
gcc	ggt	gct	ctg	acc	tgg	ctg	tcc	tgc	ggg	agc	ctg	tgc	ctg	ctg	ggg	447
Ala	G1y	Ala	Leu	Thr	Trp	Leu	Ser	Cys	G1y	Ser	Leu	Cys	Leu	Leu	Gly	
				115					120					125		
tgc			_													495
Cys	He	Ala	Gly	Cys	Cys	Phe	Tie			Cys	Val	Asp	Ala	Leu	Gln	
								369/	735							

130 135 140

gac gtg gac cat tac tgt ccc aac tgc aga gct ctc ctg ggc acc tac 543
Asp Val Asp His Tyr Cys Pro Asn Cys Arg Ala Leu Leu Gly Thr Tyr

145 150 155

aag cgt ttg taggactcag ccagacgtgg agggagccgg gtgccgcagg 592
Lys Arg Leu

160

aagteettte caceteteat eeagetteac geetggtgga ggttetgeee tggtggtete 652
aceteteeag ggggeeeace tteatgtett ettttggggg gaatacgteg caaaactaac 712
aaateteeaa aceeeagaaa ttgetgettg gagtegtgea taggaettge aaagaeatte 772
ceettgagtg teagtteeae ggttteetge etceetgaga eeetgagtee tgeeatetaa 832
ctgtgateat tgeeetaee gaatatette etgtgatetg eeateagtgg etettttte 892
ctgetteeat gggeetteet ggtggeagte teaaaetgag aageeacagt tgeettatt 952
ttgaggetgt tetgeeeaga geteggetga aceageettt agtgeetaee attatettat 1012
cegtetette eegteeetga tgacaaagat ettgeettae agaetttaea ggettggett 1072
tgagattetg taactgeaga etteattage acacagatte actttaattt ettaatttt 1132
tttttaaata caaggagggg getattaaca eeeagtaeag acatateeae aaggtegtaa 1192
370/735

atgcatgcta gaaaaatagg gctggatctt atcactgccc tgtctcccct tgtttctctg 1252

tgccagatct tcagtgcccc tttccataca gggattttt tctcatagag taattatatg 1312

aacagttttt atgacctcct tttggtctga aatactttcg aacagaattt cttttttta 1372

aaaaaaaaaca gagatgggt cttactatgt tgcccaggct ggtgtcgaac tcctgggctc 1432

aagcgatcct tctgccttgg cctcccgaag tgctgggatt gcaggcataa gctaccatgc 1492

tgggcctgaa cataatttca agaggaggat ttataaaacc attttctgta atcaaatgat 1552

tggtgtcatt ttcccatttg ccaatgtagt ctcactt 1589

<210> 107

<211> 249

<212> PRT

<213> Homo sapiens

<400> 107

Met Ala Ser Ala Ser Gly Ala Met Ala Lys His Glu Gln Ile Leu Val

1 5 10 15

Leu Asp Pro Pro Thr Asp Leu Lys Phe Lys Gly Pro Phe Thr Asp Val
20 25 30

Val Thr Thr Asn Leu Lys Leu Arg Asn Pro Ser Asp Arg Lys Val Cys 371/735

W	O 02	/0537	37												PCT/JP01/11389
		35					40					45			
Phe	-	Val	Lys	Thr	Thr		Pro	Arg	Arg	Tyr	Cys 60	Val	Arg	Pro	Asn
	50					55					00				
Ser	Gly	Ile	Ile	Asp	Pro	Gly	Ser	Thr	Val	Thr	Val	Ser	Val	Met	Leu
65					70					75					80
											٠				
Gln	Pro	Phe	Asp		Asp	Pro	Asn	Glu		Ser	Lys	His	Lys		Met
				85					90					95	
Val	Gln	Thr	Ile	Phe	Ala	Pro	Pro	Asn	Thr	Ser	Asp	Met	Glu	Ala	Val
			100					105					110		
Trp	Lys		Ala	Lys	Pro	Asp		Leu	Met	Asp	Ser	Lys	Leu	Arg	Cys
		115					120					125			
Val	Phe	Glu	Met	Pro	Asn	Glu	Asn	Asp	Lys	Leu	Asn	Asp	Met	Glu	Pro
	130					135		•			140				
Ser	Lys	Ala	Val	Pro	Leu	Asn	Ala	Ser	Lys	Gln	Asp	Gly	Pro	Met	Pro
145					150					155					160
Lve	Pro	His	Ser	Va1	Ser	I.eu	Asn	Asn	Thr	Glu	Thr	Arg	Ĭ.vs	[,e11	Met.
د ر ــ	110		201	, 41	201	Doa	.1011	TOD.	* ***	<b>5.44</b>			٠, ٥	204	

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Glu Glu Cys Lys Arg Leu Gln Gly Glu Met Met Lys Leu Ser Glu Glu

Asn Arg His Leu Arg Asp Glu Gly Leu Arg Leu Arg Lys Val Ala His
195 200 205

Ser Asp Lys Pro Gly Ser Thr Ser Thr Ala Ser Phe Arg Asp Asn Val

Thr Ser Pro Leu Pro Ser Leu Leu Val Val Ile Ala Ala Ile Phe Ile 225 230 235 240

Gly Phe Phe Leu Gly Lys Phe Ile Leu 245

<210> 108

<211> 1595

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (232).. (978)

<400> 108

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gegageetgg cetegteeta gageteggee gageegtege egeegtegte eeeegeeeee 180

agtcagcaaa ccgccgccgc gggcgcgccc ccgctctgcg ctgtctctcc g atg	gcg 237
Met	Ala
1	
1	
tcc gcc tca ggg gcc atg gcg aag cac gag cag atc ctg gtc ctc	gat 285
Ser Ala Ser Gly Ala Met Ala Lys His Glu Gln Ile Leu Val Leu	Asp
5 10 15	
	+ 200
ccg ccc aca gac ctc aaa ttc aaa ggc ccc ttc aca gat gta gtc	
Pro Pro Thr Asp Leu Lys Phe Lys Gly Pro Phe Thr Asp Val Val	Thr
20 25 30	
aca aat ctt aaa ttg cga aat cca tcg gat aga aaa gtg tgt ttc a	aaa 381
Thr Asn Leu Lys Leu Arg Asn Pro Ser Asp Arg Lys Val Cys Phe I	Lvs
35 40 45	50
30 40 40	30
gtg aag act aca gca cct cgc cgg tac tgt gtg agg ccc aac agt g	gga 429
Val Lys Thr Thr Ala Pro Arg Arg Tyr Cys Val Arg Pro Asn Ser G	Gly
55 60 65	
att att gac cca ggg tca act gtg act gtt tca gta atg cta cag o	ccc <b>4</b> 77
·	
Ile Ile Asp Pro Gly Ser Thr Val Thr Val Ser Val Met Leu Gln F	Pro
70 . 75 80	
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Phe Asp Tyr Asp Pro Asn Glu Lys Ser Lys His Lys Phe Met Val O	G1n
85 90 95	
50 50	
aca att ttt gct cca cca aac act tca gat atg gaa gct gtg tgg a	aaa 573
374/735	

Thr	Ile	Phe	Ala	Pro	Pro	Asn	Thr	Ser	Asp	Met	Glu	Ala	Val	Trp	Lys	
	100					105					110					
gag	gca	aaa	cct	gat	gaa	tta	atg	gat	tcc	aaa	ttg	aga	tgc	gta	ttt	621
Glu	Ala	Lys	Pro	Asp	Glu	Leu	Met	Asp	Ser	Lys	Leu	Arg	Cys	Val	Phe	
115					120					125					130	
gaa	atg	ccc	aat	gaa	aat	gat	aaa	ttg	aat	gat	atg	gaa	cct	agc	aaa	669
Glu	Met	Pro	Asn	Glu	Asn	Asp	Lys	Leu	Asn	Asp	Met	G1u	Pro	Ser	Lys	
				135					140					145		
gct	gtt	cca	ctg	aat	gca	tct	aag	caa	gat	gga	cct	atg	cca	aaa	cca	717
Ala	Val	Pro	Leu	Asn	Ala	Ser	Lys	G1n	Asp	Gly	Pro	Met	Pro	Lys	Pro	
			150					155					160			
cac	agt	gtt	tca	ctt	aat	gat	acc	gaa	aca	agg	aaa	cta	atg	gaa	gag	765
His	Ser	Val	Ser	Leu	Asn	Asp	Thr	Glu	Thr	Arg	Lys	Leu	Met	Glu	Glu	
		165					170					175				
tgt	aaa	aga	ctt	cag	gga	gaa	atg	atg	aag	cta	tca	gaa	gaa	aat	cgg	813
Cys	Lys	Arg	Leu	G1n	Gly	G1u	Met	Met	Lys	Leu	Ser	Glu	Glu	Asn	Arg	
	180					185					190					
cac	ctg	aga	gat	gaa	ggt	tta	agg	ctc	aga	aag	gta	gca	cat	tcg	gat	861
His	Leu	Arg	Asp	G1u	Gly	Leu	Arg	Leu	Arg	Lys	Val	Ala	His	Ser	Asp	
195					200					205					210	•
aaa	cct	gga	tca	acc	tca	act	gca	tcc	ttc	aga	gat	aat	gtc	acc	agt	909
Lys	Pro	Gly	Ser	Thr	Ser	Thr	Ala			Arg	Asp	Asn	Val	Thr	Ser	
								375/	735							

215 220 225

cct ctt cct tca ctt ctt gtt gta att gca gcc att ttc att gga ttc 957
Pro Leu Pro Ser Leu Leu Val Val Ile Ala Ala Ile Phe Ile Gly Phe
230 235 240

ttt cta ggg aaa ttc atc ttg tagagtgaag catgcagagt gctgtttctt 1008 Phe Leu Gly Lys Phe Ile Leu

245

ttttttttt tetettgace agaaaaagat ttgtttacet accatteat tggtagtatg 1068
geecaaeggtg accattttt tgtgtgtaca gegteatata ggetttgeet ttaatgatet 1128
cttaceggtta gaaaacacaa taaaaacaaa etgttegget actggacagg ttgtatatta 1188
ccagateate actageagat gteagttgea cattgagtee tttatgaaat teataaataa 1248
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cttateeett gtgaggeagt tgttgaetga gtttteate ettaeaatee tgteeeatgg 1548
tatttaacat aaaaaaaaaa aaaactgtta acagattett getegat 1595
376/735

<210> 109

<211> 540

<212> PRT

<213> Homo sapiens

<400> 109

Met Gly Thr Thr Ala Arg Ala Ala Leu Val Leu Thr Tyr Leu Ala Val

1 5 10 15

Ala Ser Ala Ala Ser Glu Gly Gly Phe Thr Ala Thr Gly Gln Arg Gln
20 25 30

Leu Arg Pro Glu His Phe Gln Glu Val Gly Tyr Ala Ala Pro Pro Ser
35 40 45

Pro Pro Leu Ser Arg Ser Leu Pro Met Asp His Pro Asp Ser Ser Gln
50 55 60

His Gly Pro Pro Phe Glu Gly Gln Ser Gln Val Gln Pro Pro Pro Ser 65 70 75 80

Gln Glu Ala Thr Pro Leu Gln Gln Glu Lys Leu Leu Pro Ala Gln Leu 85 90 95

Pro Ala Glu Lys Glu Val Gly Pro Pro Leu Pro Gln Glu Ala Val Pro 100 105 110

Leu Gln Lys Glu Leu Pro Ser Leu Gln His Pro Asn Glu Gln Lys Glu Gly Thr Pro Ala Pro Phe Gly Asp Gln Ser His Pro Glu Pro Glu Ser Trp Asn Ala Ala Gln His Cys Gln Gln Asp Arg Ser Gln Gly Gly Trp Gly His Arg Leu Asp Gly Phe Pro Pro Gly Arg Pro Ser Pro Asp Asn Leu Asn Gln Ile Cys Leu Pro Asn Arg Gln His Val Val Tyr Gly Pro Trp Asn Leu Pro Gln Ser Ser Tyr Ser His Leu Thr Arg Gln Gly Glu Thr Leu Asn Phe Leu Glu Ile Gly Tyr Ser Arg Cys Cys His Cys Arg Ser His Thr Asn Arg Leu Glu Cys Ala Lys Leu Val Trp Glu Glu Ala Met Ser Arg Phe Cys Glu Ala Glu Phe Ser Val Lys Thr Arg Pro His 

Trp Cys Cys Thr Arg Gln Gly Glu Ala Arg Phe Ser Cys Phe Gln Glu
260 265 270
378/735

Glu	Ala	Pro 275	G1n	Pro	His	Tyr	G1n 280	Leu	Arg	Ala	Cys	Pro 285	Ser	His	Gln
Pro	Asp 290	Ile	Ser	Ser	G1y	Leu 295	Glu	Leu	Pro	Phe	Pro 300	Pro	Gly	Val	Pro
Thr 305	Leu	Asp	Asn	Ile	Lys 310	Asn	Ile	Cys	His	Leu 315	Arg	Arg	Phe	Arg	Ser 320
Va1	Pro	Arg	Asn	Leu 325	Pro	Ala	Thr	Asp	Pro 330	Leu	G1n	Arg	Glu	Leu 335	Leu
Ala	Leu	Ile	G1n 340	Leu	G1u	Arg	Glu	Phe 345	Gln	Arg	Cys	Cys	Arg 350	Gln	Gly
Asn	Asn	His 355	Thr	Cys	Thr	Trp	Lys 360	Ala	Trp	G1u	Asp	Thr 365	Leu	Asp	Lys
Tyr	Cys 370	Asp	Arg	Glu	Tyr	Ala 375	Val	Lys	Thr	His	His 380	His	Leu	Cys	Cys
Arg 385	His	Pro	Pro	Ser	Pro 390	Thr	Arg	Asp	Glu	Cys 395	Phe	Ala	Arg	Arg	Ala 400
Pro	Tyr	Pro	Asn	Tyr 405	Asp	Arg	Asp	Ile	Leu 410	Thr	Ile	Asp	Ile	Gly 415	Arg

Val Thr Pro Asn Leu Met Gly His Leu Cys Gly Asn Gln Arg Val Leu 379/735

420 425 430

Thr Lys His Lys His Ile Pro Gly Leu Ile His Asn Met Thr Ala Arg
435 440 445

Cys Cys Asp Leu Pro Phe Pro Glu Gln Ala Cys Cys Ala Glu Glu Glu 450 455 460

Lys Leu Thr Phe Ile Asn Asp Leu Cys Gly Pro Arg Arg Asn Ile Trp 465 470 475 480

Arg Asp Pro Ala Leu Cys Cys Tyr Leu Ser Pro Gly Asp Glu Gln Val
485 490 495

Asn Cys Phe Asn Ile Asn Tyr Leu Arg Asn Val Ala Leu Val Ser Gly
500 505 510

Asp Thr Glu Asn Ala Lys Gly Gln Gly Glu Gln Gly Ser Thr Gly Gly
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Thr Asn Ile Ser Ser Thr Ser Glu Pro Lys Glu Glu
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<210> 110

<211> 1810

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (102).. (1721)

<400> 110

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gaggacccac ctctgagtgt ccagtggtca gttgccccag g atg ggg acc aca gcc 116

Met Gly Thr Thr Ala

1 5

aga gca gcc ttg gtc ttg acc tat ttg gct gtt gct tct gct gcc tct 164
Arg Ala Ala Leu Val Leu Thr Tyr Leu Ala Val Ala Ser Ala Ala Ser
10 15 20

gag gga ggc ttc acg gct aca gga cag agg cag ctg agg cca gag cac 212
Glu Gly Gly Phe Thr Ala Thr Gly Gln Arg Gln Leu Arg Pro Glu His
25 30 35

ttt caa gaa gtt ggc tac gca gct ccc ccc tcc cca ccc cta tcc cga 260
Phe Gln Glu Val Gly Tyr Ala Ala Pro Pro Ser Pro Pro Leu Ser Arg

40 45 50

age etc ecc atg gat eac ect gac tec tet eag eat gge ect ecc ttt 308

Ser Leu Pro Met Asp His Pro Asp Ser Ser Gln His Gly Pro Pro Phe

55 60 65

gag gga cag agt caa gtg cag ccc cct ccc tct cag gag gcc acc cct 356 Glu Gly Gln Ser Gln Val Gln Pro Pro Pro Ser Gln Glu Ala Thr Pro 381/735

70					75					80					85	
ctc	caa	cag	gaa	aag	ctg	cta	cct	gcc	caa	ctc	cct	gct	gaa	aag	gaa	404
														Lys		
DUG	0111	0111	olu	90	Боа	Dog	110	1114	95	Dou	110	1114	ozu	100	Olu	
				00					50					100		
gtg	ggt	ccc	cct	ctc	cct	cag	gaa	gct	gtc	ccc	ctc	caa	aaa	gag	ctg	452
														Glu		
			105					110					115			
															.•	
ccc	tct	ctc	cag	cac	ccc	aat	gaa	cag	aag	gaa	gga	acg	cca	gct	cca	500
														Ala		
		120					125					130				
ttt	ggg	gac	cag	agc	cat	cca	gaa	cct	gag	tcc	tgg	aat	gca	gcc	cag	548
Phe	Gly	Asp	Gln	Ser	His	Pro	Glu	Pro	G1u	Ser	Trp	Asn	Ala	Ala	G1n	
	135					140					145					
cac	tgc	caa	cag	gac	cgg	tcc	caa	ggg	ggc	tgg	ggc	cac	cgg	ctg	gat	596
His	Cys	G1n	Gln	Asp	Arg	Ser	Gln	G1y	Gly	Trp	Gly	His	Arg	Leu	Asp	
150					155					160					165	
ggc	ttc	ссс	cct	ggg	cgg	cct	tct	cca	gac	aat	ctg	aac	caa	atc	tgc	644
Gly	Phe	Pro	Pro	Gly	Arg	Pro	Ser	Pro	Asp	Asn	Leu	Asn	Gln	Ile	Cys	
				170					175	•				180		
ctt	cct	aac	cgt	cag	cat	gtg	gta	tat	ggt	ccc	tgg	aac	cta	cca	cag	692
Leu	Pro	Asn	Arg	G1n	His	Val	Val	Tyr	G1y	Pro	Trp	Asn	Leu	Pro	G1n	
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								382/	735							

WO 02/053737

PCT/JP01/11389

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Ser	Ser	Tyr	Ser	His	Leu	Thr	Arg	G1n	Gly	Glu	Thr	Leu	Asn	Phe	Leu	
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gag	att	gga	tat	tcc	cgc	tgc	tgc	cac	tgc	cgc	agc	cac	aca	aac	cgc	788
G1u	Ile	Gly	Tyr	Ser	Arg	Cys	Cys	His	Cys	Arg	Ser	His	Thr	Asn	Arg	
	215					220					225					
cta	gag	tgt	gcc	aaa	ctt	gtg	tgg	gag	gaa	gca	atg	agc	cga	ttc	tgt	836
Leu	Glu	Cys	Ala	Lys	Leu	Val	Trp	G1u	Glu	Ala	Met	Ser	Arg	Phe	Cys	
230					235					240					245	
gag	gcc	gag	ttc	tcg	gtc	aag	acc	cga	ССС	cac	tgg	tgc	tgc	acg	cgg	884
Glu	Ala	Glu	Phe	Ser	Val	Lys	Thr	Arg	Pro	His	Trp	Cys	Cys	Thr	Arg	
				250					255					260		
cag	ggg	gag	gct	cgg	ttc	tcc	tgc	ttc	cag	gag	gaa	gct	ссс	cag	cca	932
Gln	G1y	G1u	Ala	Arg	Phe	Ser	Cys	Phe	G1n	G1u	G1u	Ala	Pro	G1n	Pro	
			265					270					275			
cac	tac	cag	ctc	cgg	gcc	tgc	ссс	agc	cat [.]	cag	cct	gat	att	tcc	tcg	980
His	Tyr	Gln	Leu	Arg	Ala	Cys	Pro	Ser	His	G1n	Pro	Asp	Ile	Ser	Ser	
		280					285					290				
ggt	ctt	gag	ctg	cct	ttc	cct	cct	ggg	gtg	ссс	aca	ttg	gac	aat	atc	1028
Gly	Leu	G1u	Leu	Pro	Phe	Pro	Pro	G1y	Val	Pro	Thr	Leu	Asp	Asn	Ile	
	295					300					305					

aag	aac	atc	tgc	cac	ctg	agg	cgc	ttc	cgc	tct	gtg	cca	cgc	aac	ctg	1076
Lys	Asn	Ile	Cys	His	Leu	Arg	Arg	Phe	Arg	Ser	Val	Pro	Arg	Asn	Leu	
310					315					320					325	
cca	gct	act	gac	ссс	cta	caa	agg	gag	ctg	ctg	gca	ctg	atc	cag	ctg	1124
Pro	Ala	Thr	Asp	Pro	Leu	G1n	Arg	Glu	Leu	Leu	Ala	Leu	Ile	Gln	Leu	
				330					335					340		
gag	agg	gag	ttc	cag	cgc	tgc	tgc	cgc	cag	ggg	aac	aat	cac	acc	tgt	1172
G1u	Arg	Glu	Phe	Gln	Arg	Cys	Cys	Arg	Gln	Gly	Asn	Asn	His	Thr	Cys	
			345					350					355			
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aca	tgg	aag	gcc	tgg	gag	gat	acc	ctt	gac	aaa	tac	tgt	gac	cgg	gag	1220
Thr	Trp	Lys	Ala	Trp	Glu	Asp	Thr	Leu	Asp	Lys	Tyr	Cys	Asp	Arg	Glu	
		360					365					370				
tat	gct	gtg	aag	acc	cac	cac	cac	ttg	tgt	tgc	cgc	cac	cct	ссс	agc	1268
Tyr	Ala	Val	Lys	Thr	His	His	His	Leu	Cys	Cys	Arg	His	Pro	Pro	Ser	
	375					380					385					
cct	act	cgg	gat	gag	tgc	ttt	gcc	cgt	cgg	gct	cct	tac	ccc	aac	tat	1316
Pro	Thr	Arg	Asp	Glu	Cys	Phe	Ala	Arg	Arg	Ala	Pro	Tyr	Pro	Asn	Tyr	
390					395					400		•			405	
gac	cgg	gac	atc	ttg	acc	att	gac	atc	ggt	cga	gtc	acc	ccc	aac	ctc	1364
Asp	Arg	Asp	Ile	Leu	Thr	Ile	Asp	Ile	Gly	Arg	Val	Thr	Pro	Asn	Leu	
				410					415					420		
atg	ggc	cac	ctc	tgt	gga	aac	caa	aga	gtt	ctc	acc	aag	cat	aaa	cat	1412
				-				384/	_		-	-			-	

Met	Gly	His	Leu	Cys	Gly	Asn	Gln	Arg	Val	Leu	Thr	Lys	His	Lys	His	
			425					430					435			
att	cct	ggg	ctg	atc	cac	aac	atg	act	gcc	cgc	tgc	tgt	gac	ctg	cca	1460
Ile	Pro	Gly	Leu	Ile	His	Asn	Met	Thr	Ala	Arg	Cys	Cys	Asp	Leu	Pro	
		440					445					450				
	•															
ttt	cca	gaa	cag	gcc	tgc	tgt	gca	gag	gag	gag	aaa	tta	acc	ttc	atc	1508
Phe	Pro	G1u	Gln	Ala	Cys	Cys	Ala	Glu	Glu	Glu	Lys	Leu	Thr	Phe	Ile	
	455					460					465					
aat	gat	ctg	tgt	ggt	ссс	cga	cgt	aac	atc	tgg	cga	gac	cct	gcc	ctc	1556
Asn	Asp	Leu	Cys	Gly	Pro	Arg	Arg	Asn	Ile	Trp	Arg	Asp	Pro	Ala	Leu	
470			-		475					480					485	
tgc	tgt	tac	ctg	agt	cct	ggg	gat	gaa	cag	gtc	aac	tgc	ttc	aac	atc	1604
Cys	Cys	Tyr	Leu	Ser	Pro	Gly	Asp	Glu	Gln	Val	Asn	Cys	Phe	Asn	Ile	

aat tat ctg agg aac gtg gct cta gtg tct gga gac act gag aac gcc 1652
Asn Tyr Leu Arg Asn Val Ala Leu Val Ser Gly Asp Thr Glu Asn Ala
505 510 515

495

500

490

aag ggc cag ggg gag cag ggc tca act gga gga aca aat atc agc tcc 1700 Lys Gly Gln Gly Glu Gln Gly Ser Thr Gly Gly Thr Asn Ile Ser Ser 520 525 530

acc tct gag ccc aag gaa gaa tgagtcaccc cagagcccta gagggtcaga 1751
Thr Ser Glu Pro Lys Glu Glu

535 540

tggggggaac cccaccctgc cccacccatc tgaacactca ttacactaaa cacctcttg 1810

<210> 111

<211> 540

<212> PRT

<213> Homo sapiens

**<400> 111** .

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Ala Ser Ala Ala Ser Glu Gly Gly Phe Thr Ala Thr Gly Gln Arg Gln
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Leu Arg Pro Glu His Phe Gln Glu Val Gly Tyr Ala Ala Pro Pro Ser 35 40 45

Pro Pro Leu Ser Arg Ser Leu Pro Met Asp His Pro Asp Ser Ser Gln
50 55 60

His Gly Pro Pro Phe Glu Gly Gln Ser Gln Val Gln Pro Pro Pro Ser
65 70 75 80

Gln Glu Ala Thr Pro Leu Gln Gln Glu Lys Leu Leu Pro Ala Gln Leu 85 90 95

Pro Ala Glu Lys Glu Val Gly Pro Pro Leu Pro Gln Glu Ala Val Pro Leu Gln Lys Glu Leu Pro Ser Leu Gln His Pro Asn Glu Gln Lys Glu Gly Thr Pro Ala Pro Phe Gly Asp Gln Ser His Pro Glu Pro Glu Ser Trp Asn Ala Ala Gln His Cys Gln Gln Asp Arg Ser Gln Gly Gly Trp Gly His Arg Leu Asp Gly Phe Pro Pro Gly Arg Pro Ser Pro Asp Asn Leu Asn Gln Ile Cys Leu Pro Asn Arg Gln His Val Val Tyr Gly Pro Trp Asn Leu Pro Gln Ser Ser Tyr Ser His Leu Thr Arg Gln Gly Glu Thr Leu Asn Phe Leu Glu Ile Gly Tyr Ser Arg Cys Cys His Cys Arg Ser His Thr Asn Arg Leu Glu Cys Ala Lys Leu Val Trp Glu Glu Ala 

Met Ser Arg Phe Cys Glu Ala Glu Phe Ser Val Lys Thr Arg Pro His

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Trp	Cys	Cys	Thr 260	Arg	Gln	Gly	Glu	Ala 265	Arg	Phe	Ser	Cys	Phe 270	Gln	G1u
			200					200					210		
Glu	Ala		Gln	Pro	His	Tyr		Leu	Arg	Ala	Cys		Ser	His	Gln ·
		275					280					285			
Pro		Ile	Ser	Ser	G1y		Glu	Leu	Pro	Phe		Pro	Gly	Val	Pro
	290					295					300				
	Leu	Asp	Asn	Ile		Asn	Ile	Cys	His		Arg	Arg	Phe	Arg	
305					310			•		315					320
Val	Pro	Arg	Asn	Leu	Pro	Ala	Thr	Asp	Pro	Leu	Gln	Arg	Glu	Leu	Leu
				325					330					335	
Ala	Leu	Ile	G1n	Leu	G1u	Arg	Glu	Phe	G1n	Arg	Cys	Cys	Arg	Gln	G1y
			340					345					350		
Asn	Asn	His	Thr	Cys	Thr	Trp	Lys	Ala	Trp	G1u	Asp	Thr	Leu	Asp	Lys
		355					360					365			
Tyr	Cys	Asp	Arg	Glu	Tyr	Ala	Val	Lys	Thr	His	His	His	Leu	Cys	Cys
	370					375					380				
Arg	His	Pro	Pro	Ser	Pro	Thr	Arg	Asp	Glu	Cys	Phe	Ala	Arg	Arg	Ala
385					390					395					400
Pro	Tyr	Pro	Asn	Tyr	Asp	Arg	Asp	Ile 388/		Thr	Ile	Asp	Ile	Ser	Arg

405 410 415

Val Thr Pro Asn Leu Met Gly His Leu Cys Gly Asn Gln Arg Val Leu
420 425 430

Thr Lys His Lys His Ile Pro Gly Leu Ile His Asn Met Thr Ala Arg
435 440 445

Cys Cys Asp Leu Pro Phe Pro Glu Gln Ala Cys Cys Ala Glu Glu Glu 450 455 460

Lys Leu Thr Phe Ile Asn Asp Leu Cys Gly Pro Arg Arg Asn Ile Trp
465 470 475 480

Arg Asp Pro Ala Leu Cys Cys Tyr Leu Ser Pro Gly Asp Glu Gln Val
485
490
495

Asn Cys Phe Asn Ile Asn Tyr Leu Arg Asn Val Ala Leu Val Ser Gly 500 505 510

Asp Thr Glu Asn Ala Lys Gly Gln Gly Glu Gln Gly Ser Thr Gly Gly
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Thr Asn Ile Ser Ser Thr Ser Glu Pro Lys Glu Glu
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aga gca gcc ttg gtc ttg acc tat ttg gct gtt gct tct gct gcc tct 164 Arg Ala Ala Leu Val Leu Thr Tyr Leu Ala Val Ala Ser Ala Ala Ser 20

15

gag gga ggc ttc acg gct aca gga cag agg cag ctg agg cca gag cac 212 Glu Gly Gly Phe Thr Ala Thr Gly Gln Arg Gln Leu Arg Pro Glu His

> 25 30 35

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age etc ecc atg gat cac ect gae tec tet eag eat gge ect ecc ttt 308 Ser Leu Pro Met Asp His Pro Asp Ser Ser Gln His Gly Pro Pro Phe

55 60 65

gag	gga	cag	agt	caa	gtg	cag	ссс	cct	ccc	tct	cag	gag	gcc	acc	cct	356
Glu	Gly	Gln	Ser	Gln	Val	Gln	Pro	Pro	Pro	Ser	Gln	Glu	Ala	Thr	Pro	
70					75					80					85	
ctc	caa	cag	gaa	aag	ctg	cta	cct	gcc	caa	ctc	cct	gct	gaa	aag	gaa	404
Leu	Gln	Gln	Glu	Lys	Leu	Leu	Pro	Ala	G1n	Leu	Pro	Ala	Glu	Lys	Glu	
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gtg	ggt	ccc	cct	ctc	cct	cag	gaa	gct	gtc	ccc	ctc	caa	aaa	gag	ctg	452
Val	G1y	Pro	Pro	Leu	Pro	G1n	Glu	Ala	Val	Pro	Leu	Gln	Lys	Glu	Leu	
			105					110					115			
ccc	tct	ctc	cag	cac	ccc	aat	gaa	cag	aag	gaa	gga	acg	cca	gct	cca	500
Pro	Ser	Leu	Gln	His	Pro	Asn	Glu	G1n	Lys	Glu	Gly	Thr	Pro	Ala	Pro	
		120					125					130				
ttt	ggg	gac	cag	agc	cat	cca	gaa	cct	gag	tcc	tgg	aat	gca	gcc	cag	548
Phe	G1y	Asp	Gln	Ser	His	Pro	G1u	Pro	Glu	Ser	Trp	Asn	Ala	Ala	G1n	
	135					140					145					
cac	tgc	caa	cag	gac	cgg	tcc	caa	ggg	ggc	tgg	ggc	cac	cgg	ctg	gat	596
His	Cys	G1n	G1n	Asp	Arg	Ser	Gln	G1y	Gly	Trp	G1y	His	Arg	Leu	Asp	
150					155					160					165	
ggc	ttc	ccc	cct	ggg	cgg	cct	tct	cca	gac	aat	ctg	aac	caa	atc	tgc	644
Gly	Phe	Pro	Pro	Gly	Arg	Pro	Ser	Pro	Asp	Asn	Leu	Asn	Gln	Ile	Cys	
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Leu	Pro	Asn	Arg	Gln	His	Val	Val	Tyr	Gly	Pro	Trp	Asn	Leu	Pro	Gln	
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tcc	agc	tac	tcc	cac	ctc	act	cgc	cag	ggt	gag	acc	ctc	aat	ttc	ctg	740
Ser	Ser	Tyr	Ser	His	Leu	Thr	Arg	Gln	Gly	G1u	Thr	Leu	Asn	Phe	Leu	
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gag	att	gga	tat	tcc	cgc	tgc	tgc	cac	tgc	cgc	agc	cac	aca	aac	cgc	788
Glu	Ile	Gly	Tyr	Ser	Arg	Cys	Cys	His	Cys	Arg	Ser	His	Thr	Asn	Arg	·
	215					220					225					
cta	gag	tgt	gcc	aaa	ctt	gtg	tgg	gag	gaa	gca	atg	agc	cga	ttc	tgt	836
Leu	Glu	Cys	Ala	Lys	Leu	Val	Trp	Glu	Glu	Ala	Met	Ser	Arg	Phe	Cys	
230					235					240					245	
gag	gcc	gag	ttc	tcg	gtc	aag	acc	cga	ccc	cac	tgg	tgc	tgc	acg	cgg	884
Glu	Ala	G1u	Phe	Ser	Val	Lys	Thr	Arg	Pro	His	Trp	Cys	Cys	Thr	Arg	
				250					255					260		
cag	ggg	gag	gct	cgg	ttc	tcc	tgc	ttc	cag	gag	gaa	gct	ссс	cag	cca	932
Gln	Gly	G1u	Ala	Arg	Phe	Ser	Cys	Phe	G1n	Glu	Glu	Ala	Pro	Gln	Pro	
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cac	tac	cag	ctc	cgg	gcc	tgc	ccc	agc	cat	cag	cct	gat	att	tcc	tcg	980
His	Tyr	Gln	Leu	Arg	Ala	Cys	Pro	Ser	His	Gln	Pro	Asp	Ile	Ser	Ser	
		280					285					290				
ggt	ctt	gag	ctg	cct	ttc	cct	cct	ggg 392/		ccc	aca	ttg	gac	aat	atc	1028

Gly	Leu	Glu	Leu	Pro	Phe	Pro	Pro	Gly	Val	Pro	Thr	Leu	Asp	Asn	Ile	
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aag	aac	atc	tgc	cac	ctg	agg	cgc	ttc	cgc	tct	gtg	cca	cgc	aac	ctg	1076
Lys	Asn	Ile	Cys	His	Leu	Arg	Arg	Phe	Arg	Ser	Val	Pro	Arg	Asn	Leu	
310					315					320					325	
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cca	gct	act	gac	ccc	cta	caa	agg	gag	ctg	ctg	gca	ctg	atc	cag	ctg	1124
Pro	Ala	Thr	Asp	Pro	Leu	Gln	Arg	G1u	Leu	Leu	Ala	Leu	Ile	G1n	Leu	
				330					335					340		
gag	agg	gag	ttc	cag	cgc	tgc	tgc	cgc	cag	ggg	aac	aat	cac	acc	tgt	1172
G1u	Arg	Glu	Phe	Gln	Arg	Cys	Cys	Arg	Gln	Gly	Asn	Asn	His	Thr	Cys	
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aca	tgg	aag	gcc	tgg	gag	gat	acc	ctt	gac	aaa	tac	tgt	gac	cgg	gag	1220
Thr	Trp	Lys	Ala	Trp	Glu	Asp	Thr	Leu	Asp	Lys	Tyr	Cys	Asp	Arg	Glu	
		360					365					370				
tat	gct	gtg	aag	acc	cac	cac	cac	ttg	tgt	tgc	cgc	cac	cct	ссс	agc	1268
Tyr	Ala	Val	Lys	Thr	His	His	His	Leu	Cys	Cys	Arg	His	Pro	Pro	Ser	
	375					380					385					
cct	act	cgg	gat	gag	tgc	ttt	gcc	cgt	cgg	gct	cct	tac	ccc	aac	tat	1316
Pro	Thr	Arg	Asp	Glu	Cys	Phe	Ala	Arg	Arg	Ala	Pro	Tyr	Pro	Asn	Tyr	
390					395					400					405	
gac	cgg	gac	atc	ttg	acc	att	gac	atc	agt	cga	gtc	acc	ccc	aac	ctc	1364
Asp	Arg	Asp	Ile	Leu	Thr	Ile	Asp	Ile	Ser	Arg	Val	Thr	Pro	Asn	Leu	
								393/	735							

				410					415					420		
atg	ggc	cac	ctc	tgt	gga	aac	caa	aga	gtt	ctc	acc	aag	cat	aaa	cat	1412
Met	Gly	His	Leu	Cys	Gly	Asn	Gln	Arg	Val	Leu	Thr	Lys	His	Lys	His	
			425					430					435			
att	cct	ggg	ctg	atc	cac	aac	atg	act	gcc	cgc	tgc	tgt	gac	ctg	cca	1460
Ile	Pro	Gly	Leu	Ile	His	Asn	Met	Thr	Ala	Arg	Cys	Cys	Asp	Leu	Pro	
		440					445					450				
ttt	cca	gaa	cag	gcc	tgc	tgt	gca	gag	gag	gag	aaa	tta	acc	ttc	atc	1508
Phe	Pro	Glu	Gln	Ala	Cys	Cys	Ala	Glu	G1u	Glu	Lys	Leu	Thr	Phe	Ile	
	455					460					465					
aat	gat	ctg	tgt	ggt	ccc	cga	cgt	aac	atc	tgg	cga	gac	cct	gcc	ctc	1556
Ąsn	Asp	Leu	Cys	Gly	Pro	Arg	Arg	Asn	Ile	Trp	Arg	Asp	Pro	Ala	Leu	
470					475					480					485	
tgc	tgt	tac	ctg	agt	cct	ggg	gat	gaa	cag	gtc	aac	tgc	ttc	aac	atc	1604
Cys	Cys	Tyr	Leu	Ser	Pro	Gly	Asp	Glu	Gln	Val	Asn	Cys	Phe	Asn	Ile	
				490					495					500		
aat	tat	ctg	agg	aac	gtg	gct	cta	gtg	tct	gga	gac	act	gag	aac	gcc	1652
Asn	Tyr	Leu	Arg	Asn	Val	Ala	Leu	Val	Ser	Gly	Asp	Thr	Glu	Asn	Ala	
			505					510					515			
aag	ggc	cag	ggg	gag	cag	ggc	tca	act	gga	gga	aca	aat	atc	agc	tcc	1700

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530

Lys Gly Gln Gly Glu Gln Gly Ser Thr Gly Gly Thr Asn Ile Ser Ser

525

520

acc tot gag coc aag gaa gaa tgagtcaccc cagagcocta gagggtcaga 1751

Thr Ser Glu Pro Lys Glu Glu
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<211> 382

<212> PRT

<213> Homo sapiens

<400> 113

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Arg Ile Leu Leu Gly Thr Ala Val Glu Ser Ala Trp Gly Asp Glu
35 40 45

Gln Ser Ala Phe Arg Cys Asn Thr Gln Gln Pro Gly Cys Glu Asn Val
50 55 60

Cys Tyr Asp Lys Ser Phe Pro Ile Ser His Val Arg Phe Trp Val Leu
65 70 75 80

Gln Ile Ile Phe Val Ser Val Pro Thr Leu Leu Tyr Leu Ala His Val 85 90 95

Phe Tyr Val Met Arg Lys Glu Glu Lys Leu Asn Lys Lys Glu Glu Glu 100 105 110

Leu Lys Val Ala Gln Thr Asp Gly Val Asn Val Asp Met His Leu Lys
115 120 125

Gln Ile Glu Ile Lys Lys Phe Lys Tyr Gly Ile Glu Glu His Gly Lys 130 135 140

Val Lys Met Arg Gly Gly Leu Leu Arg Thr Tyr Ile Ile Ser Ile Leu 145 150 155 160

Phe Lys Ser Ile Phe Glu Val Ala Phe Leu Leu Ile Gln Trp Tyr Ile 165 170 175

Tyr Gly Phe Ser Leu Ser Ala Val Tyr Thr Cys Lys Arg Asp Pro Cys 180 185 190

Pro His Gln Val Asp Cys Phe Leu Ser Arg Pro Thr Glu Lys Thr Ile 195 200 205

Phe Ile Ile Phe Met Leu Val Val Ser Leu Val Ser Leu Ala Leu Asn 210 215 220

Ile Ile Glu Leu Phe Tyr Val Phe Phe Lys Gly Val Lys Asp Arg Val
225 230 235 240
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Lys	Gly	Lys	Ser	Asp	Pro	Tyr	His	Ala	Thr	Ser	Gly	Ala	Leu	Ser	Pro
				245					250					255	

- Ala Lys Asp Cys Gly Ser Gln Lys Tyr Ala Tyr Phe Asn Gly Cys Ser
  260 265 270
- Ser Pro Thr Ala Pro Leu Ser Pro Met Ser Pro Pro Gly Tyr Lys Leu 275 280 285
- Val Thr Gly Asp Arg Asn Asn Ser Ser Cys Arg Asn Tyr Asn Lys Gln
  290 295 300
- Ala Ser Glu Gln Thr Trp Ala Asn Tyr Ser Ala Glu Gln Asn Arg Met 305 310 315 320
- Gly Gln Ala Gly Ser Thr Ile Ser Asn Ser His Ala Gln Pro Phe Asp 325 330 335
- Phe Pro Asp Asp Asn Gln Asn Ser Lys Lys Leu Ala Ala Gly His Glu
  340 345 350
- Leu Gln Pro Leu Ala Ile Val Asp Gln Arg Pro Ser Ser Arg Ala Ser 355 360 365
- Ser Arg Ala Ser Ser Arg Pro Arg Pro Asp Asp Leu Glu Ile 370 375 380

<210> 114

<211> 3074

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (201).. (1346)

15

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aacagcagcg gagttttaaa ctttaaatag acaggtctga gtgcctgaac ttgccttttc 120

attttacttc atcctccaag gagttcaatc acttggcgtg acttcactac ttttaagcaa 180

aagagtggtg cccaggcaac atg ggt gac tgg agc gcc tta ggc aaa ctc ctt 233 Met Gly Asp Trp Ser Ala Leu Gly Lys Leu Leu

1 5 10

25

gac aag gtt caa gcc tac tca act gct gga ggg aag gtg tgg ctg tca 281 Asp Lys Val Gln Ala Tyr Ser Thr Ala Gly Gly Lys Val Trp Leu Ser

20

gta ctt ttc att ttc cga atc ctg ctg ctg ggg aca gcg gtt gag tca 329 Val Leu Phe Ile Phe Arg Ile Leu Leu Gly Thr Ala Val Glu Ser

30 35 40

gcc tgg gga gat gag cag tct gcc ttt cgt tgt aac act cag caa cct 377 398/735

Ala	Trp	Gly	Asp	Glu	Gln	Ser	Ala	Phe	Arg	Cys	Asn	Thr	Gln	Gln	Pro	
	45					50					55					
ggt	tgt	gaa	aat	gtc	tgc	tat	gac	aag	tct	ttc	cca	atc	tct	cat	gtg	425
Gly	Cys	Glu	Asn	Val	Cys	Tyr	Asp	Lys	Ser	Phe	Pro	Ile	Ser	His	Val	
60					65					70					75	
cgc	ttc	tgg	gtc	ctg	cag	atc	ata	ttt	gtg	tct	gta	ccc	aca	ctc	ttg	473
Arg	Phe	Trp	Val	Leu	G1n	Ile	Ile	Phe	Val	Ser	Val	Pro	Thr	Leu	Leu	
				80					85					90		
	•															
tac	ctg	gct	cat	gtg	ttc	tat	gtg	atg	cga	aag	gaa	gag	aaa	ctg	aac	521
Tyr	Leu	Ala	His	Val	Phe	Tyr	Val	Met	Arg	Lys	Glu	G1u	Lys	Leu	Asn	
			95					100					105			
aag	aaa	gag	gaa	gaa	ctc	aag	gtt	gcc	caa	act	gat	ggt	gtc	aat	gtg	569
Lys	Lys	Glu	Glu	Glu	Leu	Lys	Val	Ala	G1n	Thr	Asp	Gly	Val	Asn	Val	
		110					115					120				
gac	atg	cac	ttg	aag	cag	att	gag	ata	aag	aag	ttc	aag	tac	ggt	att	617
Asp	Met	His	Leu	Lys	Gln	Ile	Glu	Ile	Lys	Lys	Phe	Lys	Tyr	Gly	Ile	
	125					130					135					
gaa	gag	cat	ggt	aag	gtg	aaa	atg	cga	ggg	ggg	ttg	ctg	cga	acc	tac	665
Glu	Glu	His	Gly	Lys	Val	Lys	Met	Arg	Gly	Gly	Leu	Leu	Arg	Thr	Tyr	
140					145					150					155	
atc	atc	agt	atc	ctc	ttc	aag	tct	atc	ttt	gag	gtg	gcc	ttc	ttg	ctg	713
Ile	Ile	Ser	Ile	Leu	Phe	Lys	Ser			Glu	Val	Ala	Phe	Leu	Leu	
								399/	735							

				160					165					170		
atc	cag	tgg	tac	atc	tat	gga	ttc	agc	ttg	agt	gct	gtt	tac	act	tgc	761
Ile	G1n	Trp	Tyr	Ile	Tyr	Gly	Phe	Ser	Leu	Ser	Ala	Val	Tyr	Thr	Cys	
			175					180					185			
aaa	aga	gat	ccc	tgc	cca	cat	cag	gtg	gac	tgt	ttc	ctc	tct	cgc	ccc	809
Lys	Arg	Asp	Pro	Cys	Pro	His	Gln	Val	Asp	Cys	Phe	Leu	Ser	Arg	Pro	
		190					195					200				
acg	gag	aaa	acc	atc	ttc	atc	atc	ttc	atg	ctg	gtg	gtg	tcc	ttg	gtg	857
Thr	Glu	Lys	Thr	Ile	Phe	Ile	Ile	Phe	Met	Leu	Val	Va1	Ser	Leu	Val	
	205					210					215					
tcc	ctg	gcc	ttg	aat	atc	att	gaa	ctc	ttc	tat	gtt	ttc	ttc	aag	ggc	905
Ser	Leu	Ala	Leu	Asn	Ile	Ile	Glu	Leu	Phe	Tyr	Val	Phe	Phe	Lys	Gly	
220					225					230					235	
gtt	aag	gat	cgg	gtt	aag	gga	aag	agc	gac	cct	tac	cat	gcg	acc	agt	953
Val	Lys	Asp	Arg	Val	Lys	Gly	Lys	Ser	Asp	Pro	Tyr	His	Ala	Thr	Ser	
				240					245					250		
ggt	gcg	ctg	agc	cct	gcc	aaa	gac	tgt	ggg	tct	caa	aaa	tat	gct	tat	1001
Gly	Ala	Leu	Ser	Pro	Ala	Lys	Asp	Cys	Gly	Ser	Gln	Lys	Tyr	Ala	Tyr	
			255					260					265			
ttc	aat	ggc	tgc	tcc	tca	cca	acc	gct	ссс	ctc	tcg	cct	atg	tct	cct	1049
Phe	Asn	Gly	Cys	Ser	Ser	Pro	Thr	Ala	Pro	Leu	Ser	Pro	Met	Ser	Pro	

275

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280

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270

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cct	ggg	tac	aag	ctg	gtt	act	ggc	gac	aga	aac	aat	tct	tct	tgc	cgc	1097
Pro	Gly	Tyr	Lys	Leu	Val	Thr	Gly	Asp	Arg	Asn	Asn	Ser	Ser	Cys	Arg	
	285					290					295					
aat	tac	aac	aag	caa	gca	agt	gag	caa	acc	tgg	gct	aat	tac	agt	gca	1145
Asn	Tyr	Asn	Lys	Gln	Ala	Ser	Glu	Gln	Thr	Trp	Ala	Asn	Tyr	Ser	Ala	
300					305					310					315	
gaa	caa	aat	cga	atg	ggg	cag	gcg	gga	agc	acc	atc	tct	aac	tcc	cat	1193
Glu	G1n	Asn	Arg	Met	Gly	G1n	Ala	Gly	Ser	Thr	Ile	Ser	Asn	Ser	His	
				320					325					330		
gca	cag	cct	ttt	gat	ttc	ссс	gat	gat	aac	cag	aat	tct	aaa	aaa	cta	1241
Ala	Gln	Pro	Phe	Asp	Phe	Pro	Asp	Asp	Asn	Gln	Asn	Ser	Lys	Lys	Leu	
			335					340					345			
gct	gct	gga	cat	gaa	tta	cag	cca	cta	gcc	att	gtg	gac	cag	cga	cct	1289
Ala	Ala	Gly	His	Glu	Leu	Gln	Pro	Leu	Ala	Ile	Val	Asp	Gln	Arg	Pro	
		350					355					360				
tca	agc	aga	gcc	agc	agt	cgt	gcc	agc	agc	aga	cct	cgg	cct	gat	gac	1337
Ser	Ser	Arg	Ala	Ser	Ser	Arg	Ala	Ser	Ser	Arg	Pro	Arg	Pro	Asp	Asp	
	365					370					375	•				
ctg	gag	atc	taga	ataca	agg c	ttga	aago	a to	aaga	ittco	e act	tcaat	tgt			1386
Leu	Glu	Ile														
380																

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teteatggat ttttgtggtg tgggccaata tggtgtttac attatataat teetgetgtg 2346 gcaagtaaag cacacttttt ttttctccta aaatgttttt ccctgtgtat cctattatgg 2406 atactggttt tgttaattat gattetttat ttteteteet ttttttagga tatageagta 2466 atgotattac tgaaatgaat ttoottttto tgaaatgtaa toattgatgo ttgaatgata 2526 gaattttagt actgtaaaca ggctttagtc attaatgtga gagacttaga aaaaaatgct 2586 tagagtggac tattaaatgt gcctaaatga attttgcagt aactggtatt cttgggtttt 2646 cctacttaat acacagtaat tcagaacttg tattctatta tgagtttagc agtcttttgg 2706 agtgaccagc aactttgatg tttgcactaa gattttattt ggaatgcaag agaggttgaa 2766 agaggattca gtagtacaca tacaactaat ttatttgaac tatatgttga agacatctac 2826 cagtttctcc aaatgccttt tttaaaactc atcacagaag attggtgaaa atgctgagta 2886 tgacactttt cttcttgcat gcatgtcagc tacataaaca gttttgtaca atgaaaatta 2946 ctaatttgtt tgacattcca tgttaaacta cggtcatgtt cagcttcatt gcatgtaatg 3006 tagacctagt ccatcagatc atgtgttctg gagagtgttc tttattcaat aaagttttaa 3066 tttagtat 3074

<210> 115

<211> 382

<212> PRT

<213> Homo sapiens

<400> 115

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Tyr Ser Thr Ala Gly Gly Lys Val Trp Leu Ser Val Leu Phe Ile Phe
20 25 30

Arg Ile Leu Leu Gly Thr Ala Val Glu Ser Ala Trp Gly Asp Glu
35 40 45

Gln Ser Ala Phe Arg Cys Asn Thr Gln Gln Pro Gly Cys Glu Asn Val
50 55 60

Cys Tyr Asp Lys Ser Phe Pro Ile Ser His Val Arg Phe Trp Val Leu 65 70 75 80

Gln Ile Ile Phe Val Ser Val Pro Thr Leu Leu Tyr Leu Ala His Val 85 90 95

Phe Tyr Val Met Arg Lys Glu Glu Lys Leu Asn Lys Lys Glu Glu Glu 100 105 110

Leu Lys Val Ala Gln Thr Asp Gly Val Asp Wet His Leu Lys 404/735

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115 120 125

Gln Ile Glu Ile Lys Lys Phe Lys Tyr Gly Ile Glu Glu His Gly Lys 130 135 140

Val Lys Met Arg Gly Gly Leu Leu Arg Thr Tyr Ile Ile Ser Ile Leu 145 150 155 160

Phe Lys Ser Ile Phe Glu Val Ala Phe Leu Leu Ile Gln Trp Tyr Ile 165 170 175

Tyr Gly Phe Ser Leu Ser Ala Val Tyr Thr Cys Lys Arg Asp Pro Cys
180 185 190

Pro His Gln Val Asp Cys Phe Leu Ser Arg Pro Thr Glu Lys Thr Ile 195 200 205

Phe Ile Ile Phe Met Leu Val Val Ser Leu Val Ser Leu Ala Leu Asn 210 215 220

Ile Ile Glu Leu Phe Tyr Val Phe Phe Lys Gly Val Lys Asp Arg Val
225 230 235 240

Lys Gly Lys Ser Asp Pro Tyr His Ala Thr Ser Gly Ala Leu Ser Pro
245 250 255

Ala Lys Asp Cys Gly Ser Gln Lys Tyr Ala Tyr Phe Asn Gly Cys Ser 260 265 270

Ser Pro Thr Ala Pro Leu Ser Pro Met Ser Pro Pro Gly Tyr Lys Leu 275 280 285

Val Thr Gly Asp Arg Asn Asn Ser Ser Cys Arg Asn Tyr Asn Lys Gln 290 295 300

Ala Ser Glu Gln Asn Trp Ala Asn Tyr Ser Ala Glu Gln Asn Arg Met 305 310 315 320

Gly Gln Ala Gly Ser Thr Ile Ser Asn Ser His Ala Gln Pro Phe Asp 325 330 335

Phe Pro Asp Asp Asn Gln Asn Ser Lys Lys Leu Ala Ala Gly His Glu 340 345 350

Leu Gln Pro Leu Ala Ile Val Asp Gln Arg Pro Ser Ser Arg Ala Ser 355 360 365

Ser Arg Ala Ser Ser Arg Pro Arg Pro Asp Asp Leu Glu Ile 370 375 380

<210> 116

<211> 3074

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (201).. (1346)

<400> 116

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attttacttc atcctccaag gagttcaatc acttggcgtg acttcactac ttttaagcaa 180
aagagtggtg cccaggcaac atg ggt gac tgg agc gcc tta ggc aaa ctc ctt 233
Met Gly Asp Trp Ser Ala Leu Gly Lys Leu Leu

1 5 10

gac aag gtt caa gcc tac tca act gct gga ggg aag gtg tgg ctg tca 281
Asp Lys Val Gln Ala Tyr Ser Thr Ala Gly Gly Lys Val Trp Leu Ser
15 20 25

gta ctt ttc att ttc cga atc ctg ctg ctg ggg aca gcg gtt gag tca 329

Val Leu Phe Ile Phe Arg Ile Leu Leu Cly Thr Ala Val Glu Ser

30 35 40

gcc tgg gga gat gag cag tct gcc ttt cgt tgt aac act cag caa cct 377

Ala Trp Gly Asp Glu Gln Ser Ala Phe Arg Cys Asn Thr Gln Gln Pro
45

50

55

ggt tgt gaa aat gtc tgc tat gac aag tct ttc cca atc tct cat gtg 425 Gly Cys Glu Asn Val Cys Tyr Asp Lys Ser Phe Pro Ile Ser His Val 60 65 70 75

cgc	ttc	tgg	gtc	ctg	cag	atc	ata	ttt	gtg	tct	gta	ccc	aca	ctc	ttg	473
Arg	Phe	Trp	Val	Leu	Gln	Ile	Ile	Phe	Val	Ser	Val	Pro	Thr	Leu	Leu	
				80					85					90		
tac	ctg	gct	cat	gtg	ttc	tat	gtg	atg	cga	aag	gaa	gag	aaa	ctg	aac	521
Tyr	Leu	Ala	His	Val	Phe	Tyr	Val	Met	Arg	Lys	Glu	Glu	Lys	Leu	Asn	
			95					100					105			
aag	aaa	gag	gaa	gaa	ctc	aag	gtt	gcc	caa	act	gat	ggt	gtc	aat	gtg	569
Lys	Lys	Glu	Glu	Glu	Leu	Lys	Val	Ala	Gln	Thr	Asp	Gly	Val	Asn	Val	
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gac	atg	cac	ttg	aag	cag	att	gag	ata	aag	aag	ttc	aag	tac	ggt	att	617
Asp	Met	His	Leu	Lys	G1n	Ile	Glu	Ile	Lys	Lys	Phe	Lys	Tyr	Gly	Ile	
	125					130					135					
gaa	gag	cat	ggt	aag	gtg	aaa	atg	cga	ggg	ggg	ttg	ctg	cga	acc	tac	665
G1u	Glu	His	Gly	Lys	Val	Lys	Met	Arg	G1y	Gly	Leu	Leu	Arg	Thr	Tyr	
140					145					150					155	
atc	atc	agt	atc	ctc	ttc	aag	tct	atc	ttt	gag	gtg	gcc	ttc	ttg	ctg	713
Ile	Ile	Ser	Ile	Leu	Phe	Lys	Ser	Ile	Phe	Glu	Val	Ala	Phe	Leu	Leu	
				160					165					170		
atc	cag	tgg	tac	atc	tat	gga	ttc	agc	ttg	agt	gct	gtt	tac	act	tgc	761
Ile	G1n	Trp	Tyr	Ile	Tyr	Gly	Phe	Ser	Leu	Ser	Ala	Val	Tyr	Thr	Cys	
			175					180					185			
aaa	aga	gat	ccc	tgc	cca	cat	cag	gtg 408/		tgt	ttc	ctc	tct	cgc	ccc	809

Lys Arg Asp Pro Cys Pro His Gln Val Asp Cys Phe Leu Ser Arg Pro acg gag aaa acc atc ttc atc atc ttc atg ctg gtg tcc ttg gtg Thr Glu Lys Thr Ile Phe Ile Ile Phe Met Leu Val Val Ser Leu Val tcc ctg gcc ttg aat atc att gaa ctc ttc tat gtt ttc ttc aag ggc Ser Leu Ala Leu Asn Ile Ile Glu Leu Phe Tyr Val Phe Phe Lys Gly gtt aag gat cgg gtt aag gga aag agc gac cct tac cat gcg acc agt Val Lys Asp Arg Val Lys Gly Lys Ser Asp Pro Tyr His Ala Thr Ser ggt gcg ctg agc cct gcc aaa gac tgt ggg tct caa aaa tat gct tat Gly Ala Leu Ser Pro Ala Lys Asp Cys Gly Ser Gln Lys Tyr Ala Tyr ttc aat ggc tgc tcc tca cca acc gct ccc ctc tcg cct atg tct cct Phe Asn Gly Cys Ser Ser Pro Thr Ala Pro Leu Ser Pro Met Ser Pro cct ggg tac aag ctg gtt act ggc gac aga aac aat tct tct tgc cgc Pro Gly Tyr Lys Leu Val Thr Gly Asp Arg Asn Asn Ser Ser Cys Arg aat tac aac aag caa gca agt gag caa aac tgg gct aat tac agt gca Asn Tyr Asn Lys Gln Ala Ser Glu Gln Asn Trp Ala Asn Tyr Ser Ala

300					305					310					315	
gaa	caa	aat	cga	atg	ggg	cag	gcg	gga	agc	acc	atc	tct	aac	tcc	cat	1193
Glu	Gln	Asn	Arg	Met	Gly	Gln	Ala	Gly	Ser	Thr	Ile	Ser	Asn	Ser	His	
				320					325					330		
gca	cag	cct	ttt	gat	ttc	ccc	gat	gat	aac	cag	aat	tct	aaa	aaa	cta	1241
Ala	Gln	Pro	Phe	Asp	Phe	Pro	Asp	Asp	Asn	Gln	Asn	Ser	Lys	Lys	Leu	
			335					340					345			
gct	gct	gga	cat	gaa	tta	cag	cca	cta	gcc	att	gtg	gac	cag	cga	cct	1289
Ala	Ala	Gly	His	Glu	Leu	Gln	Pro	Leu	Ala	Ile	Val	Asp	G1n	Arg	Pro	
		350					355					360				
tca	agc	aga	gcc	agc	agt	cgt	gcc	agc	agc	aga	cct	cgg	cct	gat	gac	1337
Ser	Ser	Arg	Ala	Ser	Ser	Arg	Ala	Ser	Ser	Arg	Pro	Arg	Pro	Asp	Asp	
	365					370					375					
											٠					
ctg	gag	atc	taga	ataca	agg o	ttga	aago	a to	aaga	ttcc	act	caat	tgt			1386
Leu	Glu	Ile														
380																
ggaę	aaga	aa a	aagg	gtgct	g ta	igaaa	gtgc	aco	aggt	gtt	aatt	ttga	atc o	cggtg	ggaggt	1446
ggta	ctca	ac a	gcct	tatt	c at	gagg	gctta	a gaa	aaca	caa	agac	atta	iga a	ataco	taggt	1506
tcac	tggg	ggg t	gtat	gggg	gt ag	gatge	ggtgg	g aga	ıggga	ggg	gata	agag	gag g	gtgca	tgttg	1566
gtat	ttaa	ag t	agte	ggatt	c aa	agaa	ectta	ı gat	tata	aat	aaga	gtto	ca t	ttagg	gtgata	1626

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<212> PRT

<213> Homo sapiens

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Ser	Ile	Phe	Ile	G1u	Asp	Ala	Ile	Lys	Tyr	Phe	Lys	Glu	Lys	Val	Ser
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Thr	G1n	Asn	Leu	Leu	Leu	Leu	Leu	Thr	Asp	Asn	G1u	Ala	Trp	Asn	Gly
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Phe	Val	Ala	Ala	Ala	G1u	Leu	Pro	Arg	Asn	G1u	Ala	Asp	Glu	Leu	Arg
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Lys	Ala	Leu	Asp	Asn	Leu	Ala	Arg	G1n	Met	Ile	Met	Lys	Asp	Lys	Asn
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Trp	His	Asp	Lys	Gly	Gln	Gln	Tyr	Arg	Asn	Trp	Phe	Leu	Lys	Glu	Phe
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Pro	Arg	Leu	Lys	Ser	Lys	Leu	Glu	Asp	Asn	Ile	Arg	Arg	Leu	Arg	Ala
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Leu	Ala	Asp	Gly	Val 165	Gln	Lys	Val	His	Lys 170	Gly	Thr	Thr	Ile	Ala 175	Asn
Val	Val	Ser	Gly 180	Ser	Leu	Ser	Ile	Ser 185	Ser	Gly	Ile	Leu	Thr 190	Leu	Val
Gly	Met	Gly 195	Leu	Ala	Pro	Phe	Thr 200	Glu	Gly	Gly	Ser	Leu 205	Val	Leu	Leu
Glu	Pro 210	G1y	Met	Glu	Leu	Gly 215	Ile	Thr	Ala	Ala	Leu 220	Thr	Gly	Ile	Thr
Ser 225	Ser	Thr	Ile	Asp	Tyr 230	G1y	Lys	Lys	Trp.	Trp 235	Thr	G1n	Ala	Gln	Ala 240
His	Asp	Leu	Val	Ile 245	Lys	Ser	Leu	Asp	Lys 250	Leu	Lys	Glu	Val	Lys 255	G1u
Phe	Leu	Gly	G1u 260	Asn	Ile	Ser	Asn	Phe 265	Leu	Ser	Leu	Ala	Gly 270	Asn	Thr
Tyr	Gln	Leu 275	Thr	Arg	Gly	Ile	Gly 280	Lys	Asp	Ile	Arg	Ala 285	Leu	Arg	Arg
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Arg Val Thr Glu Pro Ile Ser Ala Glu Ser Gly Glu Gln Val Glu Arg

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305 310 315 320

Val Asn Glu Pro Ser Ile Leu Glu Met Ser Arg Gly Val Lys Leu Thr
325 330 335

Asp Val Ala Pro Val Ser Phe Phe Leu Val Leu Asp Val Val Tyr Leu 340 345 350

Val Tyr Glu Ser Lys His Leu His Glu Gly Ala Lys Ser Glu Thr Ala 355 360 365

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<213> Homo sapiens

<220>

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<222> (76).. (1269)

<400> 118

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Glu	Lys	Val	Ser	Thr	Gln	Asn	Leu	Leu	Leu	Leu	Leu	Thr	Asp	Asn	Glu	
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Leu	Lys	Glu	Phe	Pro	Arg	Leu	Lys	Ser	Lys	Leu	Glu	Asp	Asn	Ile	Arg	
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Arg	Leu	Arg	Ala	Leu	Ala	Asp	Gly	Val	Gln	Lys	Val	His	Lys	Gly	Thr	
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Thr	Ile	Ala	Asn	Val	Val	Ser	Gly	Ser	Leu	Ser	Ile	Ser	Ser	Gly	Ile	
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Leu	Thr	Leu	Val	Gly	Met	G1y	Leu	Ala	Pro	Phe	Thr	Glu	Gly	Gly	Ser	
	190					195					200					
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Thr	Gly	T1e	Thr	Ser	Ser	Thr	Tle	Asn	Tvr	Cl v	Lve	Lve	Trn	Trn	Thr	
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caa	gcc	caa	gcc	cac	gac	ctg	gtc	atc	aaa	agc	ctt	gac	aaa	ttg	aag	831
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Glu	Val	Lys	Glu	Phe	Leu	Gly	Glu	Asn	Ile	Ser	Asn	Phe	Leu	Ser	Leu	
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Gln	Val	Glu	Arg	Val	Asn	Glu	Pro	Ser	Ile	Leu	G1u	Met	Ser	Arg	Gly	
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at c	aag	ot o	907	as+	at a	acc	cct	σta	900	<b>+</b> +^	+++	c++	at a	cta	σat	1119
	_												_			1119
val	Lys	Leu	ınr	ASP	val	ATA	LTO	vai 418/		rne	rne	Leu	vaı	ren	лsp	

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Ser	Glu	Thr	Ala	Glu	G1u	Leu	Lys	Lys	Val	Ala	Gln	Glu	Leu	Glu	Glu	
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Glu l	Leu															
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<210> 119

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<212> PRT

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35 40 45

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Pro 145	Arg	Leu	Lys	Ser	Lys 150	Leu	Glu	Asp	Asn	Ile 155	Arg	Arg	Leu	Arg	Ala 160
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Val	Val	Ser	Gly 180	Ser	Leu	Ser	Ile	Ser 185	Ser	Gly	Ile	Leu	Thr 190	Leu	Val

Gly Met Gly Leu Ala Pro Phe Thr Glu Gly Gly Ser Leu Val Leu Leu

WO 02/053737	PCT/JP01/11389

Glu Pro Gly Met Glu Leu Gly Ile Thr Ala Ala Leu Thr Gly Ile Thr Ser Ser Thr Ile Asp Tyr Gly Lys Lys Trp Trp Thr Gln Ala Gln Ala His Asp Leu Val Ile Lys Ser Leu Asp Lys Leu Lys Glu Val Lys Glu Phe Leu Gly Glu Asn Ile Ser Asn Phe Leu Ser Leu Ala Gly Asn Thr Tyr Gln Leu Thr Arg Gly Ile Gly Lys Asp Ile Arg Ala Leu Arg Arg Ala Arg Ala Asn Leu Gln Ser Val Pro His Ala Ser Ala Ser Arg Pro Arg Val Thr Glu Pro Ile Ser Ala Glu Ser Gly Glu Gln Val Glu Arg Val Asn Glu Pro Ser Ile Leu Glu Met Ser Arg Gly Val Lys Leu Thr

Asp Val Ala Pro Val Ser Phe Phe Leu Val Leu Asp Val Val Tyr Leu 340 345 350

Val Tyr Glu Ser Lys His Leu His Glu Gly Ala Lys Ser Glu Thr Ala 355 360 365

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<222> (76).. (1269)

<400> 120

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1 5 10

tgc atc tgg atg agt gca ctt ttc ctt ggt gtg aga gtg agg gca gag 159 Cys Ile Trp Met Ser Ala Leu Phe Leu Gly Val Arg Val Arg Ala Glu

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Glu	Lys	Val	Ser	Thr	G1n	Asn	Leu	Leu	Leu	Leu	Leu	Thr	Asp	Asn	Glu	
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Ala	Trp	Asn	Gly	Phe	Val	A1a	Ala	Ala	Glu	Leu	Pro	Arg	Asn	G1u	Ala	
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Lys	Asp	Lys	Asn	Trp	His	Asp	Lys	Gly	Gln	G1n	Tyr	Arg	Asn	Trp	Phe	
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Leu	Lys	Glu	Phe	Pro	Arg	Leu	Lys	Ser	Lys	Leu	Glu	Asp	Asn	Ile	Arg	
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Arg	Leu	Arg	Ala	Leu	Ala	Asp	Gly	Val	Gln	Lys	Val	His	Lys	Gly	Thr	
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Thr	Ile	Ala	Asn	Val	Val	Ser	Gly	Ser	Leu	Ser	Ile	Ser	Ser	Gly	Ile	
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	190			-		195					200		-	•		
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						ctg										831
GIn	Ala	GIn		His	Asp	Leu	Val		Lys	Ser	Leu	Asp		Leu	Lys	
			240					245					250			
gag	gtg	aag	gag	ttt	ttg	ggt	gag	aac 425/		tcc	aac	ttt	ctt	tcc	tta	879

G1u	Val	Lys	Glu	Phe	Leu	Gly	Glu	Asn	Ile	Ser	Asn	Phe	Leu	Ser	Leu	
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Ala	Ser	Arg	Pro	Arg	Val	Thr	Glu	Pro	Ile	Ser	Ala	G1u	Ser	Gly	Glu	
				305					310					315		
cag	gtg	gag	aga	gtt	aat	gaa	ccc	agc	atc	ctg	gaa	atg	agc	aga	gga	1071
Gln	Val	Glu	Arg	Val	Asn	G1u	Pro	Ser	Ile	Leu	Glu	Met	Ser	Arg	Gly	
			320					325					330			
gtc	aag	ctc	acg	gat	gtg	gcc	cct	gta	agc	ttc	ttt	ctt	gtg	ctg	gat	1119
Val	Lys	Leu	Thr	Asp	Val	Ala	Pro	Val	Ser	Phe	Phe	Leu	Val	Leu	Asp	
		335					340					345				
gta	gtc	tac	ctc	gtg	tac	gaa	tca	aag	cac	tta	cat	gag	ggg	gca	aag	1167
Val	Val	Tyr	Leu	Val	Tyr	Glu	Ser	Lys	His	Leu	His	Glu	Gly	Ala	Lys	
	350					355					360					
														gag		1215
Ser	Glu	Thr	Ala	G1u	Glu	Leu	Lys	Lys 426/		Ala	G1n	Glu	Leu	Glu	Glu	
								720/	133							

365 370 375 380

aag cta aac att ctc aac aat aat tat aag att ctg cag gcg gac caa 1263
Lys Leu Asn Ile Leu Asn Asn Asn Tyr Lys Ile Leu Gln Ala Asp Gln
385 390 395

gaa ctg tgaccacagg gcagggcagc caccaggaga gatatgcctg gcaggggcca 1319 Glu Leu

ggacaaaatg caaactttt tttttctga gacagagtct tgctctgtcg ccaagttgca 1379
gtgagccgag atatcgccac tgcactccag cctgggtgac agagcgagac tccatctcaa 1439
aaaaaaaaaa aaaaagaata tattgacgga agaatagaga ggaggcttga aggaaccagc 1499
aatgagaagg ccaggaaaag aaagagctga aaatggagaa agcccaagag ttagaacagt 1559
tggatacagg agaagaaaca gcggctccac tacagaccca gccccaggtt caatgtcctc 1619
cgaagaatga agtcttccc tggtgatggt cccctgccct gtcttccag catccactct 1679
cccttgtcct cctgggggca tatctcagtc aggcagcgc ttcctgatga tggtcgttgg 1739
ggtggttgtc atgtgatggg tcccctccag gttactaaag ggtgcatgtc ccctgcttga 1799
acactgaagg gcaggtggtg agccatggcc atggtccca gctgaggagc aggtgtcct 1859
gagaacccaa acttcccaga gagtatgtga gaaccaacca atgaaaacag tcccatcgct 1919

cttacccggt aagtaaacag tcagaaaatt agcatgaaag cagtttagca ttgggaggaa 1979

gctcagatct ctagagctgt cttgtcccg cccaggattg acctgtgtaa gtcccaataa 2039

acteacetae teate 2054

<210> 121

<211> 108

<212> PRT

<213> Homo sapiens

<400> 121

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe

1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Phe Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys

35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala 428/735

85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
100 105

<210> 122

<211> 1546

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (89).. (412)

<400> 122

actaggcaga gccgtggaac cgccgccagg tcgctgttgg tccacgccgc ccgtcgcgcc 60

gcccgcccgc tcagcgtccg ccgccgcc atg gga gtg cag gtg gaa acc atc 112

Met Gly Val Gln Val Glu Thr Ile

1

tec cca gga gac ggg cgc acc ttc ccc aag cgc ggc cag acc tgc gtg 160

Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val

10 15 20

gtg cac tac acc ggg atg ctt gaa gat gga aag aaa ttt gat tcc tcc 208
Val His Tyr Thr Gly Met Leu Glu Asp Gly Lys Lys Phe Asp Ser Ser
25 30 35 40

cgg	gac	aga	aac	aag	ccc	ttt	aag	ttt	atg	cta	ggc	aag	cag	gag	gtg	256
Arg	Asp	Arg	Asn	Lys	Pro	Phe	Lys	Phe	Met	Leu	Gly	Lys	Gln	Glu	Val	
				45					50					55		
atc	cga	ggc	tgg	gaa	gaa	ggg	gtt	gcc	cag	atg	agt	gtg	ggt	cag	aga	304
Ile	Arg	Gly	Trp	Glu	Glu	Gly	Val	Ala	Gln	Met	Ser	Val	Gly	Gln	Arg	
			60					65					70			
gcc	aaa	ctg	act	ata	tct	cca	gat	tat	gcc	tat	ggt	gcc	act	ggg	cac	352
Ala	Lys	Leu	Thr	Ile	Ser	Pro	Asp	Tyr	Ala	Tyr	Gly	Ala	Thr	Gly	His	
		75					80					85				
cca	ggc	atc	atc	cca	cca	cat	gcc	act	ctc	gtc	ttc	gat	gtg	gag	ctt	400
Pro	Gly	Ile	Ile	Pro	Pro	His	Ala	Thr	Leu	Val	Phe	Asp	Val	Glu	Leu	
	90					95					100					
cta	aaa	ctg	gaa	tgad	agga	at g	ggcct	tcct	cc ct	tago	ctccc	tgt	tct	tgga		452
Leu	Lys	Leu	Glu													
105																
tctg	ccat	tgg a	aggga	itct	gg tg	gcctc	caga	a cat	tgtgc	aca	tgaa	tcca	ata 1	ggag	ctttt	512
ccte	atgt	ttc	cacto	cact	t te	gtata	agaca	a tci	tgccc	tga	ctga	atgt	gt 1	tctgt	cactc	572
agct	ttgo	ett d	cgac	acct	c te	gtttc	ctct	tcc	cctt	tct	ccto	gtat	gt g	gtgtt	tacct	632
aaac	tata	atg o	ccata	aacc	t ca	agtt	acto	att	ttat	ttt	gttt	tcat	tt 1	gggg	tgaag	692

attcagtttc agtcttttgg atataggttt ccaattaagt acatggtcaa gtattaacag 752 cacaagtggt aggttaacat tagaatagga attggtgttg ggggggggt ttgcaagaat 812 attttatttt aattttttgg atgaaatttt tatctattat atattaaaca ttcttgctgc 872 tgcgctgcaa agccatagca gatttgaggc gctgttgagg actgaattac tctccaagtt 932 gagagatgtc tttgggttaa attaaaagcc ctacctaaaa ctgaggtggg gatggggaga 992 gcctttgcct ccaccattcc cacccacct ccccttaaac cctctgcctt tgaaagtaga 1052 teatgtteac tgcaatgetg gacactacag gtatetgtee etgggeeage agggacetet 1112 gaageettet ttgtggeett ttttttttt teateetgtg gtttttetaa tggaetttea 1172 ggaattttgt aatctcataa ctttccaagc tccaccactt cctaaatctt aagaacttta 1232 attgacagtt tcaattgaag gtgctgtttg tagacttaac acccagtgaa agcccagcca 1292 tcatgacaaa tccttgaatg ttctcttaag aaaatgatgc tggtcatcgc agcttcagca 1352 teteetgttt tttgatgett ggeteeetet getgatetea gttteetgge tttteetee 1412 teageceett eteaeeeett tgetgteetg tgtagtgatt tggtgagaaa tegttgetge 1472 accettecce cageaceatt tatgagtete aagttttatt attgeaataa aagtgettta 1532 tgccggcttt tctc 1546

<210> 123

<211> 679

<212> PRT

<213> Homo sapiens

20

<400> 123

Met Ala Thr Leu Ile Thr Ser Thr Thr Ala Ala Thr Ala Ala Ser Gly

1 5 10 15

Pro Leu Val Asp Tyr Leu Trp Met Leu Ile Leu Gly Phe Ile Ile Ala

25

30

Phe Val Leu Ala Phe Ser Val Gly Ala Asn Asp Val Ala Asn Ser Phe

35 40 45

Gly Thr Ala Val Gly Ser Gly Val Val Thr Leu Lys Gln Ala Cys Ile

50 55 60

Leu Ala Ser Ile Phe Glu Thr Val Gly Ser Val Leu Leu Gly Ala Lys

65 70 75 80

Val Ser Glu Thr Ile Arg Lys Gly Leu Ile Asp Val Glu Met Tyr Asn

85 90 95

Ser Thr Gln Gly Leu Leu Met Ala Gly Ser Val Ser Ala Met Phe Gly

100 105 110

Ser	Ala	Val	Trp	G1n	Leu	Val	Ala	Ser	Phe	Leu	Lys	Leu	Pro	Ile	Ser
		115					120					125			
Gly	Thr	His	Cys	Ile	Val	Gly	Ala	Thr	Ile	Gly	Phe	Ser	Leu	Val	Ala
	130					135					140				
Lys	G1y	Gln	Glu	Gly	Val	Lys	Trp	Ser	Glu	Leu	Ile	Lys	Ile	Val	Met
145					150					155					160
Ser	Trp	Phe	Val	Ser	Pro	Leu	Leu	Ser	Gly	Ile	Met	Ser	Gly	Ile	Leu
				165					170					175	
Phe	Phe	Leu		Arg	Ala	Phe	Ile		His	Lys	Ala	Asp		Val	Pro
			180					185					190		
A	C1	T	A	47	T	Desa	17_1	DL -	Т	A7 -	C	T1	17 - 1	01	71 .
ASII	G1y	195	Arg	АТА	Leu	PTO	200	rne	lyr	Ата	Cys		vai	СТА	11e
		190					200					205			·
Asn	Leu	Phe	Ser	Tle	Met	Tvr	Thr	Gl v	Ala	Pro	I All	I 611	G1 v	Pho	Asn
71011	210	1110	001	110	INC 0	215		019	nia	110	220	Lea	Oly	1110	пор
Lys	Leu	Pro	Leu	Trp	Gly	Thr	Ile	Leu	Ile	Ser	Val	Gly	Cys	Ala	Val
225				•	230					235					240
Phe	Cys	Ala	Leu	Ile	Val	Trp	Phe	Phe	Val	Cys	Pro	Arg	Met	Lys	Arg
				245					250			-		255	
Lys	Ile	Glu	Arg	Glu	Ile	Lys	Cys	Ser	Pro	Ser	Glu	Ser	Pro	Leu	Met

**265** .

433/735

270

260

Glu	Lys	Lys 275	Asn	Ser	Leu	Lys	Glu 280	Asp	His	Glu	Glu	Thr 285	Lys	Leu	Ser
		2.0					200					200			
Val		Asp	Ile	G1u	Asn		His	Pro	Val	Ser	Glu	Val	Gly	Pro	Ala
	290		•			295					300				
Thr	Val	Pro	Leu	Gln	Ala	Val	Val	Glu	Glu	Arg	Thr	Val	Ser	Phe	Lys
305					310					315					320
Leu	Gly	Asp	Leu	G1u	Glu	Ala	Pro	Glu	Arg	Glu	Arg	Leu	Pro	Ser	Val
				325					330					335	٠
A	T a	T	C1	C1	TL	S	T1.	۸	C	TL	V-1	۸	C1	41-	W_1
ASP	Leu	Lys	340	Giu	Inr	ser	116	345	ser	inr	Val	ASII	350	AIS	vaı
			010					010					000		
G1n	Leu	Pro	Asn	Gly	Asn	Leu	Val	Gln	Phe	Ser	G1n	Ala	Val	Ser	Asn
		355					360					365			
G1 n	Tle	Asn	Ser	Ser	Glv	His	Tvr	Gln	Tvr	His	Thr	Va1	His	I.vs	Asn
	370				<b>-</b> _,	375	-,-		-,-		380			2,0	пор
Ser	Gly	Leu	Tyr	Lys	Glu	Leu	Leu	His	Lys	Leu	His	Leu	Ala	Lys	Val
385					390					395				,	400
C1	Asn	Cvc	Mo+	C1 v	Acn	Sor	Cl v	Acn	Lve	Pro	Leu	<b>Δ</b> *~~	A 200	Aan	1 an
ОТУ	лър	Cys	мес	405	vsħ	Ser	GIY	nsp	410	110	Leu	AI B	Arg		ASII
				400					TIV					415	

Ser Tyr Thr Ser Tyr Thr Met Ala Ile Cys Gly Met Pro Leu Asp Ser

WO 02/053737			PCT/JP01/11389
420	425	430	

Phe Arg Ala Lys Glu Gly Glu Gln Lys Gly Glu Glu Met Glu Lys Leu
435 440 445

Thr Trp Pro Asn Ala Asp Ser Lys Lys Arg Ile Arg Met Asp Ser Tyr
450 455 460

Thr Ser Tyr Cys Asn Ala Val Ser Asp Leu His Ser Ala Ser Glu Ile 465 470 475 480

Asp Met Ser Val Lys Ala Glu Met Gly Leu Gly Asp Arg Lys Gly Ser 485 490 495

Asn Gly Ser Leu Glu Glu Trp Tyr Asp Gln Asp Lys Pro Glu Val Ser 500 505 510.

Leu Leu Phe Gln Phe Leu Gln Ile Leu Thr Ala Cys Phe Gly Ser Phe
515 520 525

Ala His Gly Gly Asn Asp Val Ser Asn Ala Ile Gly Pro Leu Val Ala 530 535 540

Leu Tyr Leu Val Tyr Asp Thr Gly Asp Val Ser Ser Lys Val Ala Thr
545 550 555 560

Pro Ile Trp Leu Leu Tyr Gly Gly Val Gly Ile Cys Val Gly Leu
565 570 575

Trp Val Trp Gly Arg Arg Val Ile Gln Thr Met Gly Lys Asp Leu Thr
580 585 590

Pro Ile Thr Pro Ser Ser Gly Phe Ser Ile Glu Leu Ala Ser Ala Leu
595 600 605

Thr Val Val Ile Ala Ser Asn Ile Gly Leu Pro Ile Ser Thr Thr His
610 615 620

Cys Lys Val Gly Ser Val Val Ser Val Gly Trp Leu Arg Ser Lys Lys 625 630 635 640

Ala Val Asp Trp Arg Leu Phe Arg Asn Ile Phe Met Ala Trp Phe Val 645 650 655

Thr Val Pro Ile Ser Gly Val Ile Ser Ala Ala Ile Met Ala Ile Phe
660 665 670

Arg Tyr Val Ile Leu Arg Met 675

<210> 124

<211> 2916

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (81).. (2117)

<400> 124

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aacaaccact actccagaga atg gca acg ctg att acc agt act aca gct gct 113

Met Ala Thr Leu Ile Thr Ser Thr Thr Ala Ala

1 5 10

acc gcc gct tct ggt cct ttg gtg gac tac cta tgg atg ctc atc ctg 161

Thr Ala Ala Ser Gly Pro Leu Val Asp Tyr Leu Trp Met Leu Ile Leu

15 20 25

ggc ttc att att gca ttt gtc ttg gca ttc tcc gtg gga gcc aat gat 209

Gly Phe Ile Ile Ala Phe Val Leu Ala Phe Ser Val Gly Ala Asn Asp

30 35 40

gta gca aat tot ttt ggt aca gct gtg ggc toa ggt gta gtg acc ctg 257
Val Ala Asn Ser Phe Gly Thr Ala Val Gly Ser Gly Val Val Thr Leu
45 50 55

aag caa gcc tgc atc cta gct agc atc ttt gaa aca gtg ggc tct gtc 305 Lys Gln Ala Cys Ile Leu Ala Ser Ile Phe Glu Thr Val Gly Ser Val 60 65 70 75

tta ctg ggg gcc aaa gtg agc gaa acc atc cgg aag ggc ttg att gac 353
Leu Leu Gly Ala Lys Val Ser Glu Thr Ile Arg Lys Gly Leu Ile Asp
80 85 90

gtg	gag	atg	tac	aac	tcg	act	caa	ggg	ctg	ctg	atg	gcc	ggc	tca	gtc	401
Val	Glu	Met	Tyr	Asn	Ser	Thr	Gln	Gly	Leu	Leu	Met	Ala	Gly	Ser	Val	
			95					100					105			
agt	gct	atg	ttt	ggt	tct	gct	gtg	tgg	caa	ctc	gtg	gct	tcg	ttt	ttg	449
Ser	Ala	Met	Phe	Gly	Ser	Ala	Val	Trp	Gln	Leu	Val	Ala	Ser	Phe	Leu	
		110					115					120			•	
aag	ctc	cct	att	tct	gga	acc	cat	tgt	att	gtt	ggt	gca	act	att	ggt	497
Lys	Leu	Pro	Ile	Ser	Gly	Thr	His	Cys	Ile	Val	Gly	Ala	Thr	Ile	Gly	
	125					130					135					
ttc	tcc	ctc	gtg	gca	aag	ggg	cag	gag	ggt	gtc	aag	tgg	tct	gaa	ctg	545
Phe	Ser	Leu	Val	Ala	Lys	Gly	Gln	Glu	Gly	Val	Lys	Trp	Ser	Glu	Leu	
140					145					150					155	
ata	aaa	att	gtg	atg	tct	tgg	ttc	gtg	tcc	cca	ctg	ctt	tct	gga	att	593
Ile	Lys	Ile	Val	Met	Ser	Trp	Phe	Val	Ser	Pro	Leu	Leu	Ser	Gly	Ile	
				160					165					170		
atg	tct	gga	att	tta	ttc	ttc	ctg	gtt	cgt	gca	ttc	atc	ctc	cat	aag	641
Met	Ser	Gly	Ile	Leu	Phe	Phe	Leu	Val	Arg	Ala	Phe	Ile	Leu	His	Lys	
			175					180					185			
gca	gat	cca	gtt	cct	aat	ggt	ttg	cga	gct	ttg	cca	gtt	ttc	tat	gcc	689
Ala	Asp	Pro	Val	Pro	Asn	Gly	Leu	Arg	Ala	Leu	Pro	Val	Phe	Tyr	Ala	
		190					195					200				
tgc	aca	gtt	gga	ata	aac	ctc	ttt			atg	tat	act	gga	gca	ccg	737
								438/	135							

Cys	Thr	Val	Gly	Ile	Asn	Leu	Phe	Ser	Ile	Met	Tyr	Thr	Gly	Ala	Pro	
	205					210					215					
ttg	ctg	ggc	ttt	gac	aaa	ctt	cct	ctg	tgg	ggt	acc	atc	ctc	atc	tcg	785
Leu	Leu	Gly	Phe	Asp	Lys	Leu	Pro	Leu	Trp	Gly	Thr	Ile	Leu	Ile	Ser	
220					225					230					235	
gtg	gga	tgt	gca	gtt	ttc	tgt	gcc	ctt	atc	gtc	tgg	ttc	ttt	gta	tgt	833
Val	Gly	Cys	Ala	Val	Phe	Cys	Ala	Leu	Ile	Val	Trp	Phe	Phe	Val	Cys	
				240					245					250		
ccc	agg	atg	aag	aga	aaa	att	gaa	cga	gaa	ata	aag	tgt	agt	cct	tct	881
Pro	Arg	Met	Lys	Arg	Lys	Ile	Glu	Arg	Glu	Ile	Lys	Cys	Ser	Pro	Ser	
			255					260					265			
															•	
gaa	agc	ccc	tta	atg	gaa	aaa	aag	aat	agc	ttg	aaa	gaa	gac	cat	gaa	929
Glu	Ser	Pro	Leu	Met	Glu	Lys	Lys	Asn	Ser	Leu	Lys	Glu	Asp	His	Glu	
		270					275					280				
	aca															977
Glu	Thr	Lys	Leu	Ser	Val	-	Asp	Ile	Glu	Asn		His	Pro	Val	Ser	
	285					290					295					
	gta			•												1025
	Val	Gly	Pro	Ala		Val	Pro	Leu	GIn		Val	Val	Glu	Glu		
300				-	305					310					315	
			<b>.</b>					<b>.</b>		_						1000
•	gtc													_	_	1073
Thr	Val	Ser	Phe	Lys	Leu	Gly	Asp	Leu 439/		GIU	Ala	Pro	Glu	Arg	Glu	

				320					325					330		
auu	ctt		200	at a	gac	++ a	999	gag	gaa	200	200	ata	gat	900	acc	1121
																1121
Arg	Leu	Pro		vaı	Asp	Leu	Lys		GIU	Inr	ser	116		ser	ınr	
			335					340					345			
gtg	aat	ggt	gca	gtg	cag	ttg	cct	aat	ggg	aac	ctt	gtc	cag	ttc	agt	1169
Val	Asn	Gly	Ala	Va1	Gln	Leu	Pro	Asn	Gly	Asn	Leu	Val	Gln	Phe	Ser	
		350					355					360				
															•	
caa	gcc	gtc	agc	aac	caa	ata	aac	tcc	agt	ggc	cac	tac	cag	tat	cac	1217
G1n	Ala	Val	Ser	Asn	Gln	Ile	Asn	Ser	Ser	G1y	His	Tyr	G1n	Tyr	His	
	365					370					375					
acc	gtg	cat	aag	gat	tcc	ggc	ctg	tac	aaa	gag	cta	ctc	cat	aaa	tta	1265
Thr	Val	His	Lys	Asp	Ser	Gly	Leu	Tyr	Lys	G1u	Leu	Leu	His	Lys	Leu	
380					385					390					395	
cat	ctt	gcc	aag	gtg	gga	gat	tgc	atg	gga	gac	tcc	ggt	gac	aaa	ccc	1313
His	Leu	Ala	Lys	Val	Gly	Asp	Cys	Met	Gly	Asp	Ser	Gly	Asp	Lys	Pro	
				400					405					410		
tta	agg	cgc	aat	aat	agc	tat	act	tcc	tat	acc	atg	gca	ata	tgt	ggc	1361
Leu	Arg	Arg	Asn	Asn	Ser	Tyr	Thr	Ser	Tyr	Thr	Met	Ala	Ile	Cys	Gly	
			415					420					425			
atg	cct	ctg	gat	tca	ttc	cgt	gcc	aaa	gaa	ggt	gaa	cag	aag	ggc	gaa	1409
Met	Pro	Leu	Asp	Ser	Phe	Arg	Ala	Lys	Glu	Gly	Glu	Gln	Lys	Gly	Glu	

435

440/735

430

440

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gaa	atg	gag	aag	ctg	aca	tgg	cct	aat	gca	gac	tcc	aag	aag	cga	att	1457
Glu	Met	Glu	Lys	Leu	Thr	Trp	Pro	Asn	Ala	Asp	Ser	Lys	Lys	Arg	Ile	
	445					450					455				•	
cga	atg	gac	agt	tac	acc	agt	tac	tgc	aat	gct	gtg	tct	gac	ctt	cac	1505
Arg	Met	Asp	Ser	Tyr	Thr	Ser	Tyr	Cys	Asn	Ala	Val	Ser	Asp	Leu	His	
460					465					470					475	
tca	gca	tct	gag	ata	gac	atg	agt	gtc	aag	gca	gag	atg	ggt	cta	ggt	1553
Ser	Ala	Ser	G1u	Ile	Asp	Met	Ser	Val	Lys	Ala	Glu	Met	Gly	Leu	Gly	
				480					485					<b>49</b> 0		
gac	aga	aaa	gga	agt	aat	ggc	tct	cta	gaa	gaa	tgg	tat	gac	cag	gat	1601
Asp	Arg	Lys	Gly	Ser	Asn	Gly	Ser	Leu	Glu	Glu	Trp	Tyr	Asp	G1n	Asp	
			495					500					505			
aag	cct	gaa	gtc	tct	ctc	ctc	ttc	cag	ttc	ctg	cag	atc	ctt	aca	gcc	1649
Lys	Pro	Glu	Val	Ser	Leu	Leu	Phe	Gln	Phe	Leu	G1n	Ile	Leu	Thr	Ala	
		510					515					520				
tgc	ttt	ggg	tca	ttc	gcc	cat	ggt	ggc	aat	gac	gta	agc	aat	gcc	att	1697
Cys	Phe	Gly	Ser	Phe	Ala	His	Gly	Gly	Asn	Asp	Val	Ser	Asn	Ala	Ile	
	525					530					535					
ggg	cct	ctg	gtt	gct	tta	tat	ttg	gtt	tat	gac	aca	gga	gat	gtt	tct	1745
Gly	Pro	Leu	Val	Ala	Leu	Tyr	Leu	Val	Tyr	Asp	Thr	Gly	Asp	Val	Ser	
540					545					550					555	

tca	aaa	gtg	gca	aca	cca	ata	tgg	ctt	cta	ctc	tat	ggt	ggt	gtt	ggt	1793
Ser	Lys	Val	Ala	Thr	Pro	Ile	Trp	Leu	Leu	Leu	Tyr	Gly	Gly	Val	Gly	
				560					565					570		
atc	tgt	gtt	ggt	ctg	tgg	gtt	tgg	gga	aga	aga	gtt	atc	cag	acc	atg	1841
Ile	Cys	Val	Gly	Leu	Trp	Val	Trp	Gly	Arg	Arg	Val	Ile	Gln	Thr	Met	
			575					580					585			
										•						
ggg	aag	gat	ctg	aca	ccg	atc	aca	ccc	tct	agt	ggc	ttc	agt	att	gaa	1889
Gly	Lys	Asp	Leu	Thr	Pro	Ile	Thr	Pro	Ser	Ser	Gly	Phe	Ser	Ile	Glu	
		590					595					600				
															•	
ctg	gca	tct	gcc	ctc	act	gtg	gtg	att	gca	tca	aat	att	ggc	ctt	ccc	1937
Leu	Ala	Ser	Ala	Leu	Thr	Val	Val	Ile	Ala	Ser	Asn	Ile	Gly	Leu	Pro	
	605					610					615					
atc	agt	aca	aca	cat	tgt	aaa	gtg	ggc	tct	gtt	gtg	tct	gtt	ggc	tgg	1985
Ile	Ser	Thr	Thr	His	Cys	Lys	Val	Gly	Ser	Val	Val	Ser	Val	Gly	Trp	
620					625					630					635	
ctc	cgg	tcc	aag	aag	gct	gtt	gac	tgg	cgt	ctc	ttt	cgt	aac	att	ttt	2033
Leu	Arg	Ser	Lys		Ala	Val	Asp	Trp	Arg	Leu	Phe	Arg	Asn	Ile	Phe	
				640					645					650		
atg	gcc	tgg	ttt	gtc	aca	gtc	cct	att	tct	gga	gtt	atc	agt	gct	gcc	2081
Met	Ala	Trp	Phe	Val	Thr	Val	Pro	Ile	Ser	Gly	Val	Ile	Ser	Ala	Ala	
			655					660					665			
							•									
atc	atg	gca	atc	ttc	aga	tat	gtc			aga	atg	tgaa	gctg	tt		2127
								442/	133							

Ile Met Ala Ile Phe Arg Tyr Val Ile Leu Arg Met
670 675

tgagattaaa atttgtgtca atgtttggga ccatcttagg tattcctgct cccctgaaga 2187 atgattacag tgttaacaga agactgacaa gagtcttttt atttgggagc cagaggaggg 2247 aagtgttact tgtgctataa ctgcttttgt gctaaatatg aattgtctca aaattagctg 2307 tgtaaaatag cccgggttcc actggctcct gctgaggtcc cctttccttc tgggctgtga 2367 attectgtae atattetet actttttgta teaggettea attecattat gttttaatgt 2427 tgtctctgaa gatgacttgt gatttttttt tcttttttt aaaccatgaa gagccgtttg 2487 acagagcatg ctctgcgttg ttggtttcac cagcttctgc cctcacatgc acagggattt 2547 aacaacaaaa atataactac aacttccctt gtagtctctt atataagtag agtccttggt 2607 actetgeect cetgteagta gtggeaggat etattggeat attegggage ttettagagg 2667 gatgaggttc tttgaacaca gtgaaaattt aaattagtaa cttttttgca agcagtttat 2727 tgactgttat tgctaagaag aagtaagaaa gaaaaagcct gttggcaatc ttggttattt 2787 ctttaagatt tetggeagtg tgggatggat gaatgaagtg gaatgtgaac tttgggeaag 2847 ttaaatggga cagcetteca tgtteatttg tetacetett aactgaataa aaaageetae 2907

agtttttag 2916

<210> 125

<211> 288

<212> PRT

<213> Homo sapiens

<400> 125

Met Glu Arg Pro Gln Pro Asp Ser Met Pro Gln Asp Leu Ser Glu Ala

Leu Lys Glu Ala Thr Lys Glu Val His Thr Gln Ala Glu Asn Ala Glu

Phe Met Arg Asn Phe Gln Lys Gly Gln Val Thr Arg Asp Gly Phe Lys

Leu Val Met Ala Ser Leu Tyr His Ile Tyr Val Ala Leu Glu Glu Glu

Ile Glu Arg Asn Lys Glu Ser Pro Val Phe Ala Pro Val Tyr Phe Pro

Glu Glu Leu His Arg Lys Ala Ala Leu Glu Gln Asp Leu Ala Phe Trp

Tyr Gly Pro Arg Trp Gln Glu Val Ile Pro Tyr Thr Pro Ala Met Gln

	Arg	Tyr	Val	Lys	Arg	Leu	His	Glu	Val	Gly	Arg	Thr	Glu	Pro	Glu	Leu
			115					120					125			
	Leu	Val	Ala	His	Ala	Tyr	Thr	Arg	Tyr	Leu	Gly	Asp	Leu	Ser	Gly	Gly
		130					135					140				
(	Gln	Val	Leu	Lys	Lys	Ile	Ala	Gln	Lys	Ala	Leu	Asp	Leu	Pro	Ser	Ser
	145					150					155					160
(	Gly	Glu	Gly	Leu	Ala	Phe	Phe	Thr	Phe	Pro	Asn	Ile	Ala	Ser	Ala	Thr
					165					170					175	
]	Lys	Phe	Lys	Gln	Leu	Tyr	Arg	Ser	Arg	Met	Asn	Ser	Leu	G1u	Met	Thr
				180					185					190		
]	Pro	Ala		Arg	Gln	Arg	Val		Glu	G1u	Ala	Lys	Thr	Ala	Phe	Leu
			195					200					205			
J	Leu		Ile	G1n	Leu	Phe		Glu	Leu	Gln	Glu		Leu	Thr	His	Asp
		210					215					220				
		Lys	Asp	Gln	Ser		Ser	Arg	Ala	Pro		Leu	Arg	Gln	Arg	
4	225					230					235					240
5	Ser	Asn	Lys	Val	Gln	Asp	Ser	Ala	Pro		Glu	Thr	Pro	Arg	Gly	Lys
					245					250					255	
I	Pro	Pro	Leu	Asn	Thr	Arg	Ser	Gln	Ala	Pro	Leu	Leu	Arg	Trp	Val	Leu

260 265 270

Thr Leu Ser Phe Leu Val Ala Thr Val Ala Val Gly Leu Tyr Ala Met 275 280 285

<210> 126

<211> 1550

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (81).. (944)

<400> 126

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acgagcccag caccggccgg atg gag cgt ccg caa ccc gac agc atg ccc cag 113

Met Glu Arg Pro Gln Pro Asp Ser Met Pro Gln

5

10

25

gat ttg tca gag gcc ctg aag gag gcc acc aag gag gtg cac acc cag 161 Asp Leu Ser Glu Ala Leu Lys Glu Ala Thr Lys Glu Val His Thr Gln

20

gca gag aat gct gag ttc atg agg aac ttt cag aag ggc cag gtg acc 209
Ala Glu Asn Ala Glu Phe Met Arg Asn Phe Gln Lys Gly Gln Val Thr

30 35 40

1

15

cga	gac	ggc	ttc	aag	ctg	gtg	atg	gcc	tcc	ctg	tac	cac	atc	tat	gtg	257
Arg	Asp	Gly	Phe	Lys	Leu	Val	Met	Ala	Ser	Leu	Tyr	His	Ile	Tyr	Val	
	45					50					55					
gcc	ctg	gag	gag	gag	att	gag	cgc	aac	aag	gag	agc	cca	gtc	ttc	gcc	305
Ala	Leu	Glu	Glu	G1u	Ile	Glu	Arg	Asn	Lys	Glu	Ser	Pro	Val	Phe	Ala	
60					65					70					75	
cct	gtc	tac	ttc	cca	gaa	gag	ctg	cac	cgc	aag	gct	gcc	ctg	gag	cag	353
Pro	Val	Tyr	Phe	Pro	Glu	G1u	Leu	His	Arg	Lys	Ala	Ala	Leu	Glu	Gln	
				80					85					90		
								cgc								401
Asp	Leu	Ala		Trp	Tyr	Gly	Pro	Arg	Trp	Gln	Glu	Val		Pro	Tyr	
			95					100		•			105			
																440
								aag								449
ınr	Pro		Met	Gin	Arg	lyr		Lys	Arg	Leu	пıs		val	σιу	Arg	
		110					115					120				
202	asa	ccc	nan	o t a	c t a	ata	acc	cac	acc	tac	200	cac	tac	cta	aat	497
								cac His								431
1111	125	110	014	Leu	Deu	130	MIG	1113	MIG	1 7 1	135	ni g	1 7 1	Leu	O13	
	120					100					100					
gac	ctg	tet	ggg	ggc	cag	gtg	ctc	aaa	aag	att	gcc	cag	aaa	gcc	ctg	545
	_							Lys	_		_	_				- 23
140			,	,	145			_, -	_,_	150			-,-		155	

gac	ctg	ccc	agc	tct	ggc	gag	ggc	ctg	gcc	ttc	ttc	acc	ttc	ccc	aac	593
Asp	Leu	Pro	Ser	Ser	Gly	Glu	G1y	Leu	Ala	Phe	Phe	Thr	Phe	Pro	Asn	
				160					165					170		
att	gcc	agt	gcc	acc	aag	ttc	aag	cag	ctc	tac	cgc	tcc	cgc	atg	aac	641
Ile	Ala	Ser	Ala	Thr	Lys	Phe	Lys	G1n	Leu	Tyr	Arg	Ser	Arg	Met	Asn	
			175					180					185			
tcc	ctg	gag	atg	act	ccc	gca	gtc	agg	cag	agg	gtg	ata	gaa	gag	gcc	689
Ser	Leu	Glu	Met	Thr	Pro	Ala	Val	Arg	Gln	Arg	Val	Ile	Glu	G1u	Ala	
		190					195					200				
aag	act	gcg	ttc	ctg	ctc	aac	atc	cag	ctc	ttt	gag	gag	ttg	cag	gag	737
Lys	Thr	Ala	Phe	Leu	Leu	Asn	Ile	Gln	Leu	Phe	Glu	Glu	Leu	G1n	Glu	
	205					210					215					
ctg	ctg	acc	cat	gac	acc	aag	gac	cag	agc	ccc	tca	cgg	gca	cca	ggg	785
Leu	Leu	Thr	His	Asp	Thr	Lys	Asp	Gln	Ser	Pro	Ser	Arg	Ala	Pro	Gly	•
220					225					230					235	
ctt	cgc	cag	cgg	gcc	agc	aac	aaa	gtg	caa	gat	tct	gcc	ccc	gtg	gág	833
Leu	Arg	Gln	Arg	Ala	Ser	Asn	Lys	Val	G1n	Asp	Ser	Ala	Pro	Val	Glu	
				240					245					250		
act	ccc	aga	ggg	aag	ccc	cca	ctc	aac	acc	cgc	tcc	cag	gct	ccg	ctt	881
														Pro		
		_	255					260					265			
ctc	cga	tee	gtc	ctt	aca	ctc	agc	ttt	ctg	gtg	gcg	aca	gtt	gct	gta	929
	- 0	-00	5-5				•		/735	- •			-			

Leu Arg Trp Val Leu Thr Leu Ser Phe Leu Val Ala Thr Val Ala Val
270 275 280

ggg ctt tat gcc atg tgaatgcagg catgctggct cccagggcca tgaactttgt 984 Gly Leu Tyr Ala Met

285

ccggtggaag gccttctttc tagagaggga attctcttgg ctggcttcct taccgtgggc 1044
actgaaggct ttcagggcct ccagccctct cactgtgtcc ctctctctgg aaaggaggaa 1104
ggagcctatg gcatcttccc caacgaaaag cacatccagg caatggccta aacttcagag 1164
gggggcgaagg ggtcagccct gcccttcagc atcctcagt cctgcagcag agcctggaag 1224
acaccctaat gtggcagctg tctcaaacct ccaaaagccc tgagttcaa gtatccttgt 1284
tgacacggcc atgaccactt tccccgtggg ccatggcaat ttttacacaa acctgaaaag 1344
atgttgtgtc ttgtgtttt gtcttattt tgttggagcc actctgttcc tggctcagcc 1404
tcaaatgcag tattttgtt gtgttctgtt gtttttatag cagggttggg gtggttttg 1464
agccatgcgt gggtggggag ggaggtgtt aacggcactg tggccttggt ctaacttttg 1524
tgtgaaataa taaacaacat tgtctg

<210> 127

⟨211⟩ 135

<212> PRT

<213> Homo sapiens

<400> 127

Met Ala Cys Gly Leu Val Ala Ser Asn Leu Asn Leu Lys Pro Gly Glu 

Cys Leu Arg Val Arg Gly Glu Val Ala Pro Asp Ala Lys Ser Phe Val 

Leu Asn Leu Gly Lys Asp Ser Asn Asn Leu Cys Leu His Phe Asn Pro 

Arg Phe Asn Ala His Gly Asp Ala Asn Thr Ile Val Cys Asn Ser Lys 

Asp Gly Gly Ala Trp Gly Thr Glu Gln Arg Glu Ala Val Phe Pro Phe 

Gln Pro Gly Ser Val Ala Glu Val Cys Ile Thr Phe Asp Gln Ala Asn 

Leu Thr Val Lys Leu Pro Asp Gly Tyr Glu Phe Lys Phe Pro Asn Arg 

Leu Asn Leu Glu Ala Ile Asn Tyr Met Ala Ala Asp Gly Asp Phe Lys 

Ile Lys Cys Val Ala Phe Asp 130 135

<210> 128

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (50).. (454)

<400> 128

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Met Ala Cys

1

ggt ctg gtc gcc agc aac ctg aat ctc aaa cct gga gag tgc ctt cga 106 Gly Leu Val Ala Ser Asn Leu Asn Leu Lys Pro Gly Glu Cys Leu Arg 5 10 15

gtg cga ggc gag gtg gct cct gac gct aag agc ttc gtg ctg aac ctg 154
Val Arg Gly Glu Val Ala Pro Asp Ala Lys Ser Phe Val Leu Asn Leu
20 25 30 35

ggc aaa gac agc aac aac ctg tgc ctg cac ttc aac cct cgc ttc aac 202 Gly Lys Asp Ser Asn Asn Leu Cys Leu His Phe Asn Pro Arg Phe Asn

> 40 45 50 451/735

gcc	cac	ggc	gac	gcc	aac	acc	atc	gtg	tgc	aac	agc	aag	gac	ggc	ggg	250
Ala	His	Gly	Asp	Ala	Asn	Thr	Ile	Val	Cys	Asn	Ser	Lys	Asp	Gly	Gly	
			55					60					65			
gcc	tgg	ggg	acc	gag	cag	cgg	gag	gct	gtc	ttt	ccc	ttc	cag	cct	gga	298
Ala	Trp	Gly	Thr	Glu	Gln	Arg	Glu	Ala	Val	Phe	Pro	Phe	Gln	Pro	Gly	
		70					75					80				
agt	gtt	gca	gag	gtg	tgc	atc	acc	ttc	gac	cag	gcc	aac	ctg	acc	gtc	346
Ser	Val	Ala	Glu	Val	Cys	Ile	Thr	Phe	Asp	Gln	Ala	Asn	Leu	Thr	Val	
	85					90					95					
aag	ctg	cca	gat	gga	tac	gaa	ttc	aag	ttc	ccc	aac	cgc	ctc	aac	ctg	394
Lys	Leu	Pro	Asp	Gly	Tyr	Glu	Phe	Lys	Phe	Pro	Asn	Arg	Leu	Asn	Leu	
100					105					110					115	
gag	gcc	atc	aac	tac	atg	gca	gct	gac	ggt	gac	ttc	aag	atc	aaa	tgt	442
Glu	Ala	Ile	Asn	Tyr	Met	Ala	Ala	Asp	Gly	Asp	Phe	Lys	Ile	Lys	Cys	
				120					125					130		
gtg	gcc	ttt	gac	tgaa	atca	igc o	cagco	cate	gg co	ccca	ataa	agg	gcago	tgc		494
Val	Ala	Phe	Asp													
			135													
ctct	gcto	cc c	tg													507

<210> 129

<211> 662

<212> PRT

<213> Homo sapiens

<400> 129

Met Asn Lys Glu Ile Pro Asn Gly Asn Thr Ser Glu Leu Ile Phe Asn

1 5 10 15

Ala Val His Val Lys Asp Ala Gly Phe Tyr Val Cys Arg Val Asn Asn
20 25 30

Asn Phe Thr Phe Glu Phe Ser Gln Trp Ser Gln Leu Asp Val Cys Asp
35 40 45

Ile Pro Glu Ser Phe Gln Arg Ser Val Asp Gly Val Ser Glu Ser Lys
50 55 60

Leu Gln Ile Cys Val Glu Pro Thr Ser Gln Lys Leu Met Pro Gly Ser
65 70 75 80

Thr Leu Val Leu Gln Cys Val Ala Val Gly Ser Pro Ile Pro His Tyr

85 90 95

Gln Trp Phe Lys Asn Glu Leu Pro Leu Thr His Glu Thr Lys Lys Leu
100 105 110

Tyr Met Val Pro Tyr Val Asp Leu Glu His Gln Gly Thr Tyr Trp Cys 115 120 125

His Val Tyr Asn Asp Arg Asp Ser Gln Asp Ser Lys Lys Val Glu Ile 130 135 140

Ile Ile Gly Arg Thr Asp Glu Ala Val Glu Cys Thr Glu Asp Glu Leu 145 150 155 160

Asn Asn Leu Gly His Pro Asp Asn Lys Glu Gln Thr Thr Asp Gln Pro
165 170 175

Leu Ala Lys Asp Lys Val Ala Leu Leu Ile Gly Asn Met Asn Tyr Arg 180 185 190

Glu His Pro Lys Leu Lys Ala Pro Leu Val Asp Val Tyr Glu Leu Thr 195 200 205

Asn Leu Leu Arg Gln Leu Asp Phe Lys Val Val Ser Leu Leu Asp Leu
210 215 220

Thr Glu Tyr Glu Met Arg Asn Ala Val Asp Glu Phe Leu Leu Leu 225 230 235 240

Asp Lys Gly Val Tyr Gly Leu Leu Tyr Tyr Ala Gly His Gly Tyr Glu 245 250 255

Asn Phe Gly Asn Ser Phe Met Val Pro Val Asp Ala Pro Asn Pro Tyr
260 265 270

Arg Ser Glu Asn Cys Leu Cys Val Gln Asn Ile Leu Lys Leu Met Gln
. 275 280 285
454/735

Glu Lys Glu Thr Gly Leu Asn Val Phe Leu Leu Asp Met Cys Arg Lys 290 295 300

Arg Asn Asp Tyr Asp Asp Thr Ile Pro Ile Leu Asp Ala Leu Lys Val 305 310 315 320

Thr Ala Asn Ile Val Phe Gly Tyr Ala Thr Cys Gln Gly Ala Glu Ala 325 330 335

Phe Glu Ile Gln His Ser Gly Leu Ala Asn Gly Ile Phe Met Lys Phe 340 345 350

Leu Lys Asp Arg Leu Leu Glu Asp Lys Lys Ile Thr Val Leu Leu Asp 355 360 365

Glu Val Ala Glu Asp Met Gly Lys Cys His Leu Thr Lys Gly Lys Gln 370 375 380

Ala Leu Glu Ile Arg Ser Ser Leu Ser Glu Lys Arg Ala Leu Thr Asp 385 390 395 400

Pro Ile Gln Gly Thr Glu Tyr Ser Ala Glu Ser Leu Val Arg Asn Leu
405 410 415

Gln Trp Ala Lys Ala His Glu Leu Pro Glu Ser Met Cys Leu Lys Phe 420 425 430

Asp Cys Gly Val Gln Ile Gln Leu Gly Phe Ala Ala Glu Phe Ser Asn 455/735

WO 02/053737			PCT/JP01/11389
435	440	445	

Val Met Ile Ile Tyr Thr Ser Ile Val Tyr Lys Pro Pro Glu Ile Ile 450 455 460

Met Cys Asp Ala Tyr Val Thr Asp Phe Pro Leu Asp Leu Asp Ile Asp 465 470 475 480

Pro Lys Asp Ala Asn Lys Gly Thr Pro Glu Glu Thr Gly Ser Tyr Leu
485 490 495

Val Ser Lys Asp Leu Pro Lys His Cys Leu Tyr Thr Arg Leu Ser Ser
500 505 510

Leu Gln Lys Leu Lys Glu His Leu Val Phe Thr Val Cys Leu Ser Tyr 515 520 525

Gln Tyr Ser Gly Leu Glu Asp Thr Val Glu Asp Lys Gln Glu Val Asn 530 535 540

Val Gly Lys Pro Leu Ile Ala Lys Leu Asp Met His Arg Gly Leu Gly 545 550 555 560

Arg Lys Thr Cys Phe Gln Thr Cys Leu Met Ser Asn Gly Pro Tyr Gln
565 570 575

Ser Ser Ala Ala Thr Ser Gly Gly Ala Gly His Tyr His Ser Leu Gln 580 585 590

Asp Pro Phe His Gly Val Tyr His Ser His Pro Gly Asn Pro Ser Asn 595 600 605

Val Thr Pro Ala Asp Ser Cys His Cys Ser Arg Thr Pro Asp Ala Phe 610 615 620

Ile Ser Ser Phe Ala His His Ala Ser Cys His Phe Ser Arg Ser Asn 625 630 635 640

Val Pro Val Glu Thr Thr Asp Glu Ile Pro Phe Ser Phe Ser Asp Arg
645 650 655

Leu Arg Ile Ser Glu Lys 660

<210> 130

<211> 2251

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (74).. (2059)

<400> 130

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tcagtggttc aaa atg aat aaa gag att cca aat gga aat aca tca gag 109 457/735

Met Asn Lys Glu Ile Pro Asn Gly Asn Thr Ser Glu

1 5 10

ctt att ttt aat gca gtg cat gta aaa gat gca ggc ttt tat gtc tgt 157
Leu Ile Phe Asn Ala Val His Val Lys Asp Ala Gly Phe Tyr Val Cys
15 20 25

cga gtt aat aac aat ttc acc ttt gaa ttc agc cag tgg tca cag ctg 205
Arg Val Asn Asn Asn Phe Thr Phe Glu Phe Ser Gln Trp Ser Gln Leu
30 35 40

gat gtt tgc gac atc cca gag agc ttc cag aga agt gtt gat ggc gtc 253
Asp Val Cys Asp Ile Pro Glu Ser Phe Gln Arg Ser Val Asp Gly Val
45 50 55 60

tct gaa tcc aag ttg caa atc tgt gtt gaa cca act tcc caa aag ctg 301 Ser Glu Ser Lys Leu Gln Ile Cys Val Glu Pro Thr Ser Gln Lys Leu 65 70 75

atg cca ggc agc aca ttg gtt tta cag tgt gtt gct gtt gga agc cct 349

Met Pro Gly Ser Thr Leu Val Leu Gln Cys Val Ala Val Gly Ser Pro

80 85 90

att cct cac tac cag tgg ttc aaa aat gaa tta cca tta aca cat gag 397

Ile Pro His Tyr Gln Trp Phe Lys Asn Glu Leu Pro Leu Thr His Glu
95 100 105

acc aaa aag cta tac atg gtg cct tat gtg gat ttg gaa cac caa gga 445
Thr Lys Lys Leu Tyr Met Val Pro Tyr Val Asp Leu Glu His Gln Gly
458/735

WO 02/053737			PCT/JP01/11389
110	115	120	

acc	tac	tgg	tgt	cat	gta	tat	aat	gat	cga	gac	agt	caa	gat	agc	aag	493
Thr	Tyr	Trp	Cys	His	Val	Tyr	Asn	Asp	Arg	Asp	Ser	Gln	Asp	Ser	Lys	
125					130					135					140	
aag	gta	gaa	atc	atc	ata	gga	aga	aca	gat	gag	gca	gtg	gag	tgc	act	541
Lys	Val	Glu	Ile	Ile	Ile	Gly	Arg	Thr	Asp	Glu	Ala	Val	Glu	Cys	Thr	
				145					150					155		
															•	
gaa	gat	gaa	tta	aat	aat	ctt	ggt	cat	cct	gat	aat	aaa	gag	caa	aca	589
Glu	Asp	G1u	Leu	Asn	Asn	Leu	Gly	His	Pro	Asp	Asn	Lys	G1u	G1n	Thr	
			160					165					170			
act	gac	cag	cct	ttg	gcg	aag	gac	aag	gtt	gcc	ctt	ttg	ata	gga	aat	637
Thr	Asp	G1n	Pro	Leu	Ala	Lys	Asp	Lys	Val	Ala	Leu	Leu	Ile	Gly	Asn	
		175					180					185				
atg	aat	tac	cgg	gag	cac	ссс	aag	ctc	aaa	gct	cct	ttg	gtg	gat	gtg	685
Met	Asn	Tyr	Arg	Glu	His	Pro	Lys	Leu	Lys	Ala	Pro	Leu	Val	Asp	Val	
	190					195					200					
tac	gaa	ttg	act	aac	tta	ctg	aga	cag	ctg	gac	ttc	aaa	gtg	gtt	tca	733

Tyr Glu Leu Thr Asn Leu Leu Arg Gln Leu Asp Phe Lys Val Val Ser 

ctg ttg gat ctt act gaa tat gag atg cgt aat gct gtg gat gag ttt Leu Leu Asp Leu Thr Glu Tyr Glu Met Arg Asn Ala Val Asp Glu Phe 

tta	ctc	ctt	tta	gac	aag	gga	gta	tat	ggg	tta	tta	tat	tat	gca	gga	829
Leu	Leu	Leu	Leu	Asp	Lys	Gly	Val	Tyr	Gly	Leu	Leu	Tyr	Tyr	Ala	Gly	
			240					245					250			
cat	ggt	tat	gaa	aat	ttt	ggg	aac	agc	ttc	atg	gtc	ccc	gtt	gat	gct	877
His	G1y	Tyr	Glu	Asn	Phe	Gly	Asn	Ser	Phe	Met	Val	Pro	Val	Asp	Ala	
		255					260					265				
cca	aat	cca	tat	agg	tct	gaa	aat	tgt	ctg	tgt	gta	caa	aat	ata	ctg	925
Pro	Asn	Pro	Tyr	Arg	Ser	Glu	Asn	Cys	Leu	Cys	Va1	Gln	Asn	Ile	Leu	
	270					275					280					
aaa	ttg	atg	caa	gaa	aaa	gaa	act	gga	ctt	aat	gtg	ttc	tta	ttg	gat	973
Lys	Leu	Met	Gln	G1u	Lys	G1u	Thr	Gly	Leu	Asn	Va1	Phe	Leu	Leu	Asp	
285					290					295					300	
atg	tgt	agg	aaa	aga	aat	gac	tac	gat	gat	acc	att	cca	atc	ttg	gat	1021
Met	Cys	Arg	Lys	Arg	Asn	Asp	Tyr	Asp	Asp	Thr	Ile	Pro	Ile	Leu	Asp	
				305					310					315		
gca	cta	aaa	gtc	acc	gcc	aat	att	gtg	ttt	gga	tat	gcc	acg	tgt	caa	1069
Ala	Leu	Lys	Val	Thr	Ala	Asn	Ile	Val	Phe	Gly	Tyr	Ala	Thr	Cys	Gln	
			320					325					330			
gga	gca	gaa	gct	ttt	gaa	atc	cag	cat	tct	gga	ttg	gca	aat	gga	atc	1117
Gly	Ala	Glu	Ala	Phe	Glu	Ile	Gln	His	Ser	Gly	Leu	Ala	Asn	Gly	Ile	
		335					340					345				

ttt	atg	aaa	ttt	tta	aaa	gac	aga	tta	tta	gaa	gat	aag	aaa	atc	act	1165
Phe	Met	Lys	Phe	Leu	Lys	Asp	Arg	Leu	Leu	Glu	Asp	Lys	Lys	Ile	Thr	
	350					355					360					
gtg	tta	ctg	gat	gaa	gtt	gca	gaa	gat	atg	ggt	aag	tgt	cac	ctt	acc	1213
Val	Leu	Leu	Asp	Glu	Val	Ala	Glu	Asp	Met	Gly	Lys	Cys	His	Leu	Thr	
365					370					375					380	
aaa	ggc	aaa	cag	gct	cta	gag	att	cga	agt	agt	tta	tct	gag	aag	aga	1261
Lys	Gly	Lys	Gln	Ala	Leu	Glu	Ile	Arg	Ser	Ser	Leu	Ser	G1u	Lys	Arg	
				385					390					395		
gca	ctt	act	gat	cca	ata	cag	gga	aca	gaa	tat	tct	gct	gaa	tct	ctt	1309
Ala	Leu	Thr	Asp	Pro	Ile	G1n	Gly	Thr	Glu	Tyr	Ser	Ala	Glu	Ser	Leu	
			400					405					410			
gtg	cgg	aat	cta	cag	tgg	gcc	aag	gct	cat	gaa	ctt	cca	gaa	agt	atg	1357
Val	Arg	Asn	Leu	G1n	Trp	Ala	Lys	Ala	His	G1u	Leu	Pro	Glu	Ser	Met	
		415					420					425				
tgt	ctt	aag	ttt	gac	tgt	ggt	gtt	cag	att	caa	tta	gga	ttt	gca	gct	1405
Cys	Leu	Lys	Phe	Asp	Cys	Gly	Val	Gln	Ile	Gln	Leu	Gly	Phe	Ala	Aļa	
	430					435					440					
gag	ttt	tcc	aat	gtc	atg	atc	atc	tat	aca	agt	ata	gtt	tac	aaa	cca	1453
Glu	Phe	Ser	Asn	Val	Met	Ile	Ile	Tyr	Thr	Ser	Ile	Val	Tyr	Lys	Pro	
445					450					455					460	
ccg	gag	ata	ata	atg	tgt	gat	gcc	tac 461/		act	gat	ttt	cca	ctt	gat	1501
								40 I /	133							

Pro Glu Ile Ile Met Cys Asp Ala Tyr Val Thr Asp Phe Pro Leu Asp cta gat att gat cca aaa gat gca aat aaa ggc aca cct gaa gaa act Leu Asp Ile Asp Pro Lys Asp Ala Asn Lys Gly Thr Pro Glu Glu Thr ggc agc tac ttg gta tca aag gat ctt ccc aag cat tgc ctc tat acc Gly Ser Tyr Leu Val Ser Lys Asp Leu Pro Lys His Cys Leu Tyr Thr aga ctc agt tca ctg caa aaa tta aag gaa cat cta gtc ttc aca gta Arg Leu Ser Ser Leu Gln Lys Leu Lys Glu His Leu Val Phe Thr Val tgt tta tca tat cag tac tca gga ttg gaa gat act gta gag gac aag Cys Leu Ser Tyr Gln Tyr Ser Gly Leu Glu Asp Thr Val Glu Asp Lys cag gaa gtg aat gtt ggg aaa cct ctc att gct aaa tta gac atg cat Gln Glu Val Asn Val Gly Lys Pro Leu Ile Ala Lys Leu Asp Met His cga ggt ttg gga agg aag act tgc ttt caa act tgt ctt atg tct aat Arg Gly Leu Gly Arg Lys Thr Cys Phe Gln Thr Cys Leu Met Ser Asn ggt cct tac cag agt tct gca gcc acc tca gga gga gca ggg cat tat Gly Pro Tyr Gln Ser Ser Ala Ala Thr Ser Gly Gly Ala Gly His Tyr 462/735

575 580 585 cac tca ttg caa gac cca ttc cat ggt gtt tac cat tca cat cct ggt 1885 His Ser Leu Gln Asp Pro Phe His Gly Val Tyr His Ser His Pro Gly 590 595 600 1933 aat cca agt aat gtt aca cca gca gat agc tgt cat tgc agc cgg act Asn Pro Ser Asn Val Thr Pro Ala Asp Ser Cys His Cys Ser Arg Thr 605 620 610 615 cca gat gca ttt att tca agt ttc gct cac cat gct tca tgt cat ttt 1981 Pro Asp Ala Phe Ile Ser Ser Phe Ala His His Ala Ser Cys His Phe 625 630 635 agt aga agt aat gtg cca gta gag aca act gat gaa ata cca ttt agt 2029 Ser Arg Ser Asn Val Pro Val Glu Thr Thr Asp Glu Ile Pro Phe Ser 645 640 650 ttc tct gac agg ctc aga att tct gaa aaa tgacctcctt gtttttgaaa 2079 Phe Ser Asp Arg Leu Arg Ile Ser Glu Lys 655 660 gttagcataa ttttagatgc ctgtgaaata gtactgcact tacataaagt gagacattgt 2139 gaaaaggcaa atttgtatat gtagagaaag aatagtagta actgtttcat agcaaacttc 2199

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2251

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aggactttga gatgttgaaa ttacattatt taattacaga cttcctcttt ct

<210> 131 <211> 824 <212> PRT <213> Homo sapiens <400> 131 Met Ser Leu Leu Gly Asp Pro Leu Gln Ala Leu Pro Pro Ser Ala Ala Pro Thr Gly Pro Leu Leu Ala Pro Pro Ala Gly Ala Thr Leu Asn Arg Leu Arg Glu Pro Leu Leu Arg Arg Leu Ser Glu Leu Leu Asp Gln Ala Pro Glu Gly Arg Gly Trp Arg Arg Leu Ala Glu Leu Ala Gly Ser Arg Gly Arg Leu Arg Leu Ser Cys Leu Asp Leu Glu Gln Cys Ser Leu Lys Val Leu Glu Pro Glu Gly Ser Pro Ser Leu Cys Leu Leu Lys Leu Met Gly Glu Lys Gly Cys Thr Val Thr Glu Leu Ser Asp Phe Leu Gln Ala Met Glu His Thr Glu Val Leu Gln Leu Leu Ser Pro Pro Gly Ile Lys

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Ile	Thr 130	Val	Asn	Pro	G1u	Ser 135	Lys	Ala	Val	Leu	Ala 140	Gly	Gln	Phe	Val
Lys 145	Leu	Cys	Cys	Arg	Ala 150	Thr	Gly	His	Pro	Phe 155	Val	Gln	Tyr	Gln	Trp 160
Phe	Lys	Met	Asn	Lys 165	Glu	Ile	Pro	Asn	Gly 170	Asn	Thr	Ser	Glu	Leu 175	Ile
Phe	Asn	Ala	Val 180	His	Val	Lys	Asp	Ala 185	Gly	Phe	Tyr	Val	Cys 190	Arg	Val
Asn	Asn	Asn 195	Phe	Thr	Phe	Glu	Phe 200	Ser	Gln	Trp	Ser	Gln 205	Leu	Asp	Val
Cys	Asp 210	Íle	Pro	Glu	Ser	Phe 215	G1n	Arg	Ser	Val	Asp 220	G1y	Val	Ser	Glu
Ser 225	Lys	Leu	Gln	Ile	Cys 230	Val	Glu	Pro	Thr	Ser 235	G1n	Lys	Leu	Met	Pro 240
G1y	Ser	Thr	Leu	Val 245	Leu	G1n	Cys	Val	Ala 250	Val	G1y	Ser	Pro	Ile 255	Pro
His	Tyr	Gln	Trp 260	Phe	Lys	Asn	Glu	Leu 265	Pro	Leu	Thr	His	G1u 270	Thr	Lys

Lys Leu Tyr Met Val Pro Tyr Val Asp Leu Glu His Gln Gly Thr Tyr

275 280 285

Trp Cys His Val Tyr Asn Asp Arg Asp Ser Gln Asp Ser Lys Lys Val 290 295 300

Glu Ile Ile Ile Gly Arg Thr Asp Glu Ala Val Glu Cys Thr Glu Asp 305 310 315 320

Glu Leu Asn Asn Leu Gly His Pro Asp Asn Lys Glu Gln Thr Thr Asp 325 330 335

Gln Pro Leu Ala Lys Asp Lys Val Ala Leu Leu Ile Gly Asn Met Asn
340 345 350

Tyr Arg Glu His Pro Lys Leu Lys Ala Pro Leu Val Asp Val Tyr Glu 355 360 365

Leu Thr Asn Leu Leu Arg Gln Leu Asp Phe Lys Val Val Ser Leu Leu 370 375 380

Asp Leu Thr Glu Tyr Glu Met Arg Asn Ala Val Asp Glu Phe Leu Leu 385 390 395 400

Leu Leu Asp Lys Gly Val Tyr Gly Leu Leu Tyr Tyr Ala Gly His Gly
405 410 415

Tyr Glu Asn Phe Gly Asn Ser Phe Met Val Pro Val Asp Ala Pro Asn 420 425 430

Pro	Tyr		Ser	Glu	Asn	Cys		Cys	Val	Gln	Asn		Leu	Lys	Leu
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Met		G1u	Lys	Glu	Thr		Leu	Asn	Val	Phe		Leu	Asp	Met	Cys
	450					455					460				
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465					470					475					480
Lys	Val	Thr	Ala	Asn	Ile	Val	Phe	Gly	Tyr	Ala	Thr	Cys	Gln	Gly	Ala
				485					490					495	
Glu	Ala	Phe	Glu	Ile	Gln	His	Ser	Gly	Leu	Ala	Asn	G1y	Ile	Phe	Met
			500					505					510		
Lvs	Phe	I.eu	Ĭ.vs	Asp	Arø	Leu	Leu	Glu	Asn	Lvs	Lvs	Tle	Thr	Val	Leu
2,0		515	2,0	Пор			520			_,-	-,,	525			
_				4.7	63			<b>01</b>			***	-	<b></b>	-	
Leu	Asp 530	GŢĦ	Val	Ala	GLu	Asp 535	Met	GLY	Lys	Cys	His 540	Leu	Ihr	Lys	GTA
	323														
Lys	Gln	Ala	Leu	Glu	Ile	Arg	Ser	Ser	Leu	Ser	Glu	Lys	Arg	Ala	Leu

Thr Asp Pro Ile Gln Gly Thr Glu Tyr Ser Ala Glu Ser Leu Val Arg
565 570 575

555

560

550

545

Asn Leu Gln Trp Ala Lys Ala His Glu Leu Pro Glu Ser Met Cys Leu
580 585 590
467/735

Lys Phe Asp Cys Gly Val Gln Ile Gln Leu Gly Phe Ala Ala Glu Phe
595 600 605

Ser Asn Val Met Ile Ile Tyr Thr Ser Ile Val Tyr Lys Pro Pro Glu 610 615 620

Ile Ile Met Cys Asp Ala Tyr Val Thr Asp Phe Pro Leu Asp Leu Asp 625 630 635 640

Ile Asp Pro Lys Asp Ala Asn Lys Gly Thr Pro Glu Glu Thr Gly Ser
645 650 655

Tyr Leu Val Ser Lys Asp Leu Pro Lys His Cys Leu Tyr Thr Arg Leu 660 665 670

Ser Ser Leu Gln Lys Leu Lys Glu His Leu Val Phe Thr Val Cys Leu 675 680 685

Ser Tyr Gln Tyr Ser Gly Leu Glu Asp Thr Val Glu Asp Lys Gln Glu 690 695 700

Val Asn Val Gly Lys Pro Leu Ile Ala Lys Leu Asp Met His Arg Gly 705 710 715 720

Leu Gly Arg Lys Thr Cys Phe Gln Thr Cys Leu Met Ser Asn Gly Pro
725 730 735

Tyr Gln Ser Ser Ala Ala Thr Ser Gly Gly Ala Gly His Tyr His Ser 468/735

740 745 750

Leu Gln Asp Pro Phe His Gly Val Tyr His Ser His Pro Gly Asn Pro
755 760 765

Ser Asn Val Thr Pro Ala Asp Ser Cys His Cys Ser Arg Thr Pro Asp 770 775 780

Ala Phe Ile Ser Ser Phe Ala His His Ala Ser Cys His Phe Ser Arg
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Ser Asn Val Pro Val Glu Thr Thr Asp Glu Ile Pro Phe Ser Phe Ser 805 810 815

Asp Arg Leu Arg Ile Ser Glu Lys 820

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ggg	cggg	cgg	gagcı	cceg	gc a	gtcc	ggggt	t cg	ccgg	cgag	ggc	Me	t Sea		g ttg 1 Leu	176
													1			
ggg	gac	ccg	cta	cag	gcc	ctg	ccg	ccc	tcg	gcc	gcc	ccc	acg	ggg	ccg	224
Gly	Asp	Pro	Leu	Gln	Ala	Leu	Pro	Pro	Ser	Ala	Ala	Pro	Thr	Gly	Pro	
5					10					15					20	
ctg	ctc	gcc	cct	ccg	gcc	ggc	gcg	acc	ctc	aac	cgc	ctg	cgg	gag	ccg	272
			Pro													
				25		•			30					35		
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Leu	Leu	Arg	Arg	Leu	Ser	Glu	Leu	Leu	Asp	Gln	Ala	Pro	Glu	Gly	Arg	
	-		40					45					50			
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G1у	Trp	Arg	Arg	Leu	Ala	Glu	Leu	Ala	Gly	Ser	Arg	Gly	Arg	Leu	Arg	
		55					60					65				
ctc	agt	tgc	cta	gac	ctg	gag	cag	tgt	tct	ctt	aag	gta	ctg	gag	cct	416
Leu	Ser	Cys	Leu	Asp	Leu	Glu	Gln	Cys	Ser	Leu	Lys	Val	Leu	Glu	Pro	
	70					75					80					
gaa	gga	agc	ccc	agc	ctg	tgt	ctg	ctg	aag	tta	atg	ggt	gaa	aaa	ggt	464
G1u	Gly	Ser	Pro	Ser	Leu	Cys	Leu	Leu 470	-	Leu	Met	G1y	G1u	Lys	Gly	

85					90					95					100	
<b>.</b>					**~	s+		++-	.+~		ant.	n+~	<b>~~</b>	000	oot.	512
								ttc								512
Cys	Thr	Val	Thr	Glu	Leu	Ser	Asp	Phe	Leu	Gln	Ala	Met	Glu	His	Thr	
				105					110					115		
gaa	gtt	ctt	cag	ctt	ctc	agc	ccc	cca	gga	ata	aag	att	act	gta	aac	560
Glu	Val	Leu	Gln	Leu	Leu	Ser	Pro	Pro	Gly	Ile	Lys	Ile	Thr	Val	Asn	
			120					125					130			
cca	gag	tca	aag	gca	gtc	ttg	gct	gga	cag	ttt	gtg	aaa	ctg	tgt	tgc	608
Pro	Glu	Ser	Lys	Ala	Val	Leu	Ala	Gly	Gln	Phe	Val	Lys	Leu	Cys	Cys	
		135					140					145				
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Arg	Ala	Thr	Gly	His	Pro	Phe	Val	G1n	Tyr	Gln	Trp	Phe	Lys	Met	Asn	
	150					155					160					
ลลล	<b>ຜ</b> ສ ຜ	att	cca	aat	σσa	aat	aca	tca	៤១៤	ctt	att	ttt	aat	gca	gtg.	704
								Ser							_	
-	GIU	116	110	VSII		VOII	1111	261	UIU		116	1 116	ASII	AIG		
165					170					175					180	
cat	gta	aaa	gat	gca	ggc	ttt	tat	gtc	tgt	cga	gtt	aat	aac	aat	ttc	752
His	Val	Lys	Asp	Ala	Gly	Phe	Tyr	Val	Cys	Arg	Val	Asn	Asn	Asn	Phe	
				185					190					195	-	
acc	ttt	gaa	ttc	agc	cag	tgg	tca	cag	ctg	gat	gtt	tgc	gac	atc	cca	800
Thr	Phe	Glu	Phe	Ser	G1n	Trp	Ser	Gln	Leu	Asp	Val	Cys	qaA	Ile	Pro	
			200					205					210			
								471	/735							

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gag	agc	ttc	cag	aga	agt	gtt	gat	ggc	gtc	tct	gaa	tcc	aag	ttg	caa	848
Glu	Ser	Phe	Gln	Arg	Ser	Val	Asp	Gly	Val	Ser	Glu	Ser	Lys	Leu	Gln	
		215					220					225				
atc	tgt	gtt	gaa	cca	act	tcc	caa	aag	ctg	atg	cca	ggc	agc	aca	ttg	896
Ile	Cys	Val	Glu	Pro	Thr	Ser	Gln	Lys	Leu	Met	Pro	Gly	Ser	Thr	Leu	
	230					235					240					
gtt	tta	cag	tgt	gtt	gct	gtt	gga	agc	cct	att	cct	cac	tac	cag	tgg	944
Val	Leu	Gln	Cys	Val	Ala	Val	Gly	Ser	Pro	Ile	Pro	His	Tyr	Gln	Trp	
245					250					255					260	
ttc	aaa	aat	gaa	tta	cca	tta	aca	cat	gag	acc	aaa	aag	cta	tac	atg	992
Phe	Lys	Asn	Glu	Leu	Pro	Leu	Thr	His	Glu	Thr	Lys	Lys	Leu	Tyr	Met	
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gtg	cct	tat	gtg	gat	ttg	gaa	cac	caa	gga	acc	tac	tgg	tgt	cat	gta	1040
Val	Pro	Tyr	Val	Asp	Leu	Glu	His	Gln	Gly	Thr	Tyr	Trp	Cys	His	Val	
			280					285					290			
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Tyr	Asn	Asp	Arg	Asp	Ser	G1n	Asp	Ser	Lys	Lys	Val	Glu	Ile	Ile	Ile	
		295					300					305				
gga	aga	aca	gat	gag	gca	gtg	gag	tgc	act	gaa	gat	gaa	tta	aat	aat	1136
Gly	Arg	Thr	Asp	Glu	Ala	Val	G1u	Cys	Thr	Glu	Asp	Glu	Leu	Asn	Asn	
	310					315					320					

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ctt	ggt	cat	cct	gat	aat	aaa	gag	caa	aca	act	gac	cag	cct	ttg	gcg	1184
Leu	Gly	His	Pro	Asp	Asn	Lys	Glu	G1n	Thr	Thr	Asp	Gln	Pro	Leu	Ala	
325					330					335					340	
aag	gac	aag	gtt	gcc	ctt	ttg	ata	gga	aat	atg	aat	tac	cgg	gag	cac	1232
Lys	Asp	Lys	Val	Ala	Leu	Leu	Ile	Gly	Asn	Met	Asn	Tyr	Arg	Glu	His	
				345					350					355		
ccc	aag	ctc	aaa	gct	cct	ttg	gtg	gat	gtg	tac	gaa	ttg	act	aac	tta	1280
Pro	Lys	Leu	Lys	Ala	Pro	Leu	Val	Asp	Val	Tyr	Glu	Leu	Thr	Asn	Leu	
			360					365					370			
ctg	aga	cag	ctg	gac	ttc	aaa	gtg	gtt	tca	ctg	ttg	gat	ctt	act	gaa	1328
Leu	Arg	G1n	Leu	Asp	Phe	Lys	Val	Val	Ser	Leu	Leu	Asp	Leu	Thr	Glu	
		375					380					385				
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Tyr	Glu	Met	Arg	Asn	Ala	Val	Asp	G1u	Phe	Leu	Leu	Leu	Leu	Asp	Lys	
	390					395					400					
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Gly	Val	Tyr	Gly	Leu	Leu	Tyr	Tyr	Ala	Gly	His	Gly	Tyr	Glu	Asn	Phe	
405					410					415					420	
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Gly	Asn	Ser	Phe	Met	Val	Pro	Val	Asp	Ala	Pro	Asn	Pro	Tyr	Arg	Ser	
				425					430					435		
gaa	aat	tgt	ctg	tgt	gta	caa	aat			aaa	ttg	atg	caa	gaa	aaa	1520
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Glu	Asn	Cys		Cys	Val	Gln	Asn		Leu	Lys	Leu	Met		Glu	Lys	
			440					445					450			
_ଫ ጻጻ	act	បូបឧ	ctt	aat	σtσ	ttc	tta	t.t.ø	gat	ato	tgt	ឧଟଟ	ลลล	ลฮล	aat	1568
											Cys					1000
Old	1111	455	Deu	NSII	141	THE	460	Dou	nsp	mc c	0,5	465	L) 3	шБ	71311	
		100					400					100				
gac	tac	gat	gat	acc	att	cća	atc	ttg	gat	gca	cta	aaa	gtc	acc	gcc	1616
Asp	Tyr	Asp	Asp	Thr	Ile	Pro	Ile	Leu	Asp	Ala	Leu	Lys	Val	Thr	Ala	
	470					475					480					
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aat	att	gtg	ttt	gga	tat	gcc	acg	tgt	caa	gga	gca	gaa	gct	ttt	gaa	1664
Asn	Ile	Val	Phe	Gly	Tyr	Ala	Thr	Cys	Gln	Gly	Ala	Glu	Ala	Phe	Glu	
485					490					495					500	
atc	cag	cat	tct	gga	ttg	gca	aat	gga	atc	ttt	atg	aaa	ttt	tta	aaa	1712
Ile	Gln	His	Ser	Gly	Leu	Ala	Asn	Gly	Ile	Phe	Met	Lys	Phe	Leu	Lys	
				505					510					515		
gac	aga	tta	tta	gaa	gat	aag	aaa	atc	act	gtg	tta	ctg	gat	gaa	gtt	1760
Asp	Arg	Leu	Leu	Glu	Asp	Lys	Lys	Ile	Thr	Val	Leu	Leu	Asp	Glu	Val	
			520					525					530			
gca	gaa	gat	atg	ggt	aag	tgt	cac	ctt	acc	aaa	ggc	aaa	cag	gct	cta	1808
Ala	Glu	Asp	Met	Gly	Lys	Cys	His	Leu	Thr	Lys	Gly	Lys	Gln	Ala	Leu	
		535					540					545				
gag	att	cga	agt	agt	tta	tct	gag	aag	aga	gca	ctt	act	gat	cca	ata	1856
Glu	Ile	Arg	Ser	Ser	Leu	Ser	Glu	Lys 474/		Ala	Leu	Thr	Asp	Pro	Ile	

WO 02/053737 PCT/JP01/11389 cag gga aca gaa tat tct gct gaa tct ctt gtg cgg aat cta cag tgg Gln Gly Thr Glu Tyr Ser Ala Glu Ser Leu Val Arg Asn Leu Gln Trp gcc aag gct cat gaa ctt cca gaa agt atg tgt ctt aag ttt gac tgt Ala Lys Ala His Glu Leu Pro Glu Ser Met Cys Leu Lys Phe Asp Cys ggt gtt cag att caa tta gga ttt gca gct gag ttt tcc aat gtc atg Gly Val Gln Ile Gln Leu Gly Phe Ala Ala Glu Phe Ser Asn Val Met atc atc tat aca agt ata gtt tac aaa cca ccg gag ata ata atg tgt Ile Ile Tyr Thr Ser Ile Val Tyr Lys Pro Pro Glu Ile Ile Met Cys gat gcc tac gtt act gat ttt cca ctt gat cta gat att gat cca aaa Asp Ala Tyr Val Thr Asp Phe Pro Leu Asp Leu Asp Ile Asp Pro Lys 

gat gca aat aaa ggc aca cct gaa gaa act ggc agc tac ttg gta tca 2144
Asp Ala Asn Lys Gly Thr Pro Glu Glu Thr Gly Ser Tyr Leu Val Ser
645 650 655 660

aag gat ctt ccc aag cat tgc ctc tat acc aga ctc agt tca ctg caa 2192

Lys Asp Leu Pro Lys His Cys Leu Tyr Thr Arg Leu Ser Ser Leu Gln

665 670 675

475/735

aaa	tta	aag	gaa	cat	cta	gtc	ttc	aca	gta	tgt	tta	tca	tat	cag	tac	2240
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			680					685					690			
tca	gga	ttg	gaa	gat	act	gta	gag	gac	aag	cag	gaa	gtg	aat	gtt	ggg	2288
Ser	Gly	Leu	Glu	Asp	Thr	Val	Glu	Asp	Lys	Gln	G1u	Val	Asn	Val	Gly	
		695					700					705				
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Lys	Pro	Leu	Ile	Ala	Lys	Leu	Asp	Met	His	Arg	Gly	Leu	Gly	Arg	Lys	
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Thr	Cys	Phe	Gln	Thr	Cys	Leu	Met	Ser	Asn	Gly	Pro	Tyr	Gln	Ser	Ser	
725					730					735					740	
gca	gcc	acc	tca	gga	gga	gca	ggg	cat	tat	cac	tca	ttg	caa	gac	cca	2432
Ala	Ala	Thr	Ser	Gly	Gly	Ala	Gly	His	Tyr	His	Ser	Leu	Gln	Asp	Pro	
				745					750					755		
ttc	cat	ggt	gtt	tac	cat	tca	cat	cct	ggt	aat	cca	agt	aat	gtt	aca	2480
Phe	His	Gly	Val	Tyr	His	Ser	His	Pro	Gly	Asn	Pro	Ser	Asn	Val	Thr	
			760					765					770			
cca	gca	gat	agc	tgt	cat	tgc	agc	cgg	act	cca	gat	gca	ttt	att	tca	2528
Pro	Ala	Asp	Ser	Cys	His	Cys	Ser	Arg	Thr	Pro	Asp	Ala	Phe	Ile	Ser	
		775					780					785				

agt ttc gct cac cat gct tca tgt cat ttt agt aga agt aat gtg cca 2576

Ser Phe Ala His His Ala Ser Cys His Phe Ser Arg Ser Asn Val Pro
790 795 800

gta gag aca act gat gaa ata cca ttt agt ttc tct gac agg ctc aga 2624 Val Glu Thr Thr Asp Glu Ile Pro Phe Ser Phe Ser Asp Arg Leu Arg 805 810 815 820

att tot gaa aaa tgacctcott gtttttgaaa gttagcataa ttttagatgc 2676 Ile Ser Glu Lys

ctgtgaaata gtactgcact tacataaagt gagacattgt gaaaaggcaa atttgtatat 2736

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<210> 133

<211> 919

<212> PRT

<213> Homo sapiens

<400> 133

Met Lys Val Ala Arg Phe Gln Lys Ile Pro Asn Gly Glu Asn Glu Thr

1 5 10 15

Met Ile Pro Val Leu Thr Ser Lys Lys Ala Ser Glu Leu Pro Val Ser
20 25 30

Glu	Val	Ala	Ser	Ile	Leu	Gln	Ala	Asp	Leu	Gln	Asn	G1y	Leu	Asn	Lys
		35					40					45			
0	01	W - 1	<b>C</b> .	13.	<b>A</b>	<b>4</b>	41-	nt.	TT: _	01	<b>~</b>	<b>A</b>	01	DI	
Cys		vaı	ser	HIS	Arg		Ala	rne	nıs	СТА		ASI	Glu	rne	ASP
	50					55					60				
Ile	Ser	Glu	Asp	Glu	Pro	Leu	Trp	Lys	Lys	Tyr	Ile	Ser	Gln	Phe	Lys
65					70					75					80
Asn	Pro	Leu	Ile	Met	Leu	Leu	Leu	Ala	Ser	Ala	Val	Ile	Ser	Val	Leu
				85					90					95	
Met	His	Gln	Phe	Asp	Asp	Ala	Val	Ser	Ile	Thr	Val	Ala	Ile	Leu	Ile
			100					105					110		
Val	Val	Thr	Val	Ala	Phe	Val	Gln	Glu	Tyr	Arg	Ser	Glu	Lys	Ser	Leu
		115					120					125			
Glu	Glu	Leu	Ser	Lys	Leu	Val	Pro	Pro	Glu	Cys	His	Cys	Val	Arg	Glu
	130					135					140				
Gly	Lys	Leu	Glu	His	Thr	Leu	Ala	Arg	Asp	Leu	Val	Pro	Gly	Asp	Thr
145	•				150					155					160
Val	Cys	Leu	Ser	Val	Gly	Asp	Arg	Val	Pro	Ala	Asp	Leu	Arg	Leu	Phe
				165					170					175	
Glu	Ala	Val	Asp	Leu	Ser	Ile	Asp	G1u	Ser	Ser	Leu	Thr	Gly	G1u	Thr

WO 02/053	737			PCT/JP01/11389
	180	185	190	

Thr Pro Cys Ser Lys Val Thr Ala Pro Gln Pro Ala Ala Thr Asn Gly
195 200 205

Asp Leu Ala Ser Arg Ser Asn Ile Ala Phe Met Gly Thr Leu Val Arg 210 215 220

Cys Gly Lys Ala Lys Gly Val Val Ile Gly Thr Gly Glu Asn Ser Glu 225 230 235 240

Phe Gly Glu Val Phe Lys Met Met Gln Ala Glu Glu Ala Pro Lys Thr
245 250 255

Pro Leu Gln Lys Ser Met Asp Leu Leu Gly Lys Gln Leu Ser Phe Tyr 260 265 270

Ser Phe Gly Ile Ile Gly Ile Ile Met Leu Val Gly Trp Leu Leu Gly 275 280 285 .

Lys Asp Ile Leu Glu Met Phe Thr Ile Ser Val Ser Leu Ala Val Ala 290 295 300

Ala Ile Pro Glu Gly Leu Pro Ile Val Val Thr Val Thr Leu Ala Leu 305 310 315 320

Gly Val Met Arg Met Val Lys Lys Arg Ala Ile Val Lys Lys Leu Pro 325 330 335

Ile	Val	G1u		Leu	Gly	Cys	Cys		Val	Ile	Cys	Ser		Lys	Thr
			340					345					350		
Gly	Thr	Leu	Thr	Lys	Asn	Glu	Met	Thr	Val	Thr	His	Ile	Phe	Thr	Ser
		355					360					365			
Asp	Gly	Leu	His	Ala	Glu	Val	Thr	Gly	Val	Gly	Tyr	Asn	Gln	Phe	Gly
	370					375					380				
Glu	Val	Ile	Val	Asp	Gly	Asp	Val	Val	His	Gly	Phe	Tyr	Asn	Pro	Ala
385					390					395					400
Val	Ser	Arø	Tle	Val	G1u	Ala	Gl v	Cvs	Va1	Cvs	Asn	Asp	Ala	Va1	Tle
, 41	501			405	010		01,	0,5	410	2,2		,		415	
<b>A</b> -	<b>A</b>	•	<b>7</b> 1 -	T	M - 4	<b>01</b>	T	D	T1	01	01	A 7 -	T	T1 -	47 -
Arg	Asn	Asn	1hr 420	Leu	Met	Gly	Lys	Pro 425	Inr	GIU	СІУ	Ala	430	TTE	Ala
Leu	Ala	Met 435	Lys	Met	Gly	Leu	Asp 440	Gly	Leu	Gln	Gln	Asp 445	Tyr	Ile	Arg
		400					110					110			
Lys	Ala	G1u	Tyr	Pro	Phe		Ser	Glu	Gln	Lys		Met	Ala	Val	Lys
	450					455					460				
Cys	Val	His	Arg	Thr	Gln	G1n	Asp	Arg	Pro	Glu	Ile	Cys	Phe	Met	Lys
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Gly	Ala	Tyr	Glu	Gln	Val	Ile	Lys	Tyr	Cys	Thr	Thr	Tyr	G1n	Ser	Lys

490

480/735

485

495

Gly	Gln	Thr	Leu	Thr	Leu	Thr	Gln	Gln	Gln	Arg	Asp	Val	Tyr	Gln	Gln
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Glu	Lys	Ala	Arg	Met	Gly	Ser	Ala	Gly	Leu	Arg	Val	Leu	Ala	Leu	Ala
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Ser	Gly	Pro	Glu	Leu	Gly	Gln	Leu	Thr	Phe	Leu	Gly	Leu	Val	Gly	Ile
	530					535					540				
Ile	Asp	Pro	Pro	Arg	Thr	Gly	Val	Lys	Glu	Ala	Val	Thr	Thr	Leu	Ile
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Ala	Ser	G1y	Val	Ser	Ile	Lys	Met	Ile	Thr	Gly	Asp	Ser	G1n	G1u	Thr
				565					570					575	•
Ala	Val	Ala		Ala	Ser	Arg	Leu		Leu	Tyr	Ser	Lys		Ser	G1n
			580					585					590		٠
Ser	Val		Gly	G1u	G1u	Ile		Ala	Met	Asp	Val		G1n	Leu	Ser
		595					600					605			
G1n	Ile	Va1	Pro	Lys	Val	Ala	Val	Phe	Tyr	Arg	Ala	Ser	Pro	Arg	His
	610					615					620				
Lys	Met	Lys	Ile	Ile	Lys	Ser	Leu	Gln	Lys	Asn	Gly	Ser	Val	Val	Ala
625					630					635					640

Met Thr Gly Asp Gly Val Asn Asp Ala Val Ala Leu Lys Ala Ala Asp

WO 02/053737	PCT/JP01/11389
	•

650

655

Ile Gly Val Ala Met Gly Gln Thr Gly Thr Asp Val Cys Lys Glu Ala
660 665 670

645

Ala Asp Met Ile Leu Val Asp Asp Phe Gln Thr Ile Met Ser Ala 675 680 685

Ile Glu Glu Gly Lys Gly Ile Tyr Asn Asn Ile Lys Asn Phe Val Arg
690 695 700

Phe Gln Leu Ser Thr Ser Ile Ala Ala Leu Thr Leu Ile Ser Leu Ala 705 710 715 720

Thr Leu Met Asn Phe Pro Asn Pro Leu Asn Ala Met Gln Ile Leu Trp
725 730 735

Ile Asn Ile Ile Met Asp Gly Pro Pro Ala Gln Ser Leu Gly Val Glu
740 745 750

Pro Val Asp Lys Asp Val Ile Arg Lys Pro Pro Arg Asn Trp Lys Asp 755 760 765

Ser Ile Leu Thr Lys Asn Leu Ile Leu Lys Ile Leu Val Ser Ser Ile 770 775 780

Ile Ile Val Cys Gly Thr Leu Phe Val Phe Trp Arg Glu Leu Arg Asp
785 790 795 800

Asn Val Ile Thr Pro Arg Asp Thr Thr Met Thr Phe Thr Cys Phe Val 805 810 815

Phe Phe Asp Met Phe Asn Ala Leu Ser Ser Arg Ser Gln Thr Lys Ser 820 825 830

Val Phe Glu Ile Gly Leu Cys Ser Asn Arg Met Phe Cys Tyr Ala Val 835 840 845

Leu Gly Ser Ile Met Gly Gln Leu Leu Val Ile Tyr Phe Pro Pro Leu 850 855 860

Gln Lys Val Phe Gln Thr Glu Ser Leu Ser Ile Leu Asp Leu Leu Phe 865 870 875 880

Leu Leu Gly Leu Thr Ser Ser Val Cys Ile Val Ala Glu Ile Ile Lys 885 890 895

Lys Val Glu Arg Ser Arg Glu Lys Ile Gln Lys His Val Ser Ser Thr 900 905 910

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gageaggete eegectegea eegetgeece gegageaget eetetetee egaggegege 180

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ctttggatge tgetgetagg ggtggtggga geageegtgg gaegegtgge egggageggg 300

ggtgacagee tgggatteeg ggggettete tteettgtee teeteetee etetetatte 360

ceagtgtgge egtggetgae actaaagaet ttgtageeat eaaceegagt geagttega 420

tggaaa atg aag gtt gea egt ttt eaa aaa ata eet aat ggt gaa aat 468

Met Lys Val Ala Arg Phe Gln Lys Ile Pro Asn Gly Glu Asn

1 5 10

gag aca atg att cct gta ttg aca tca aaa aaa gca agt gaa tta cca 516
Glu Thr Met Ile Pro Val Leu Thr Ser Lys Lys Ala Ser Glu Leu Pro
15 20 25 30

gtc agt gaa gtt gca agc att ctc caa gct gat ctt cag aat ggt cta 564 484/735

Val	Ser	Glu	Val	Ala	Ser	Ile	Leu	Gln	Ala	Asp	Leu	Gln	Asn	Gly	Leu	
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							•									
aac	aaa	tgt	gaa	gtt	agt	cat	agg	cga	gcc	ttt	cat	ggc	tgg	aat	gag	612
Asn	Lys	Cys	Glu	Val	Ser	His	Arg	Arg	Ala	Phe	His	Gly	Trp	Asn	Glu	
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ttt	gat	att	agt	gaa	gat	gag	cca	ctg	tgg	aag	aag	tat	att	tct	cag	660
Phe	Asp	Ile	Ser	G1u	Asp	Glu	Pro	Leu	Trp	Lys	Lys	Tyr	Ile	Ser	Gln	
		65					70					75				
ttt	aaa	aat	ccc	ctt	att	atg	ctg	ctt	ctg	gct	tct	gca	gtc	atc	agt	708
Phe	Lys	Asn	Pro	Leu	Ile	Met	Leu	Leu	Leu	Ala	Ser	Ala	Val	Ile	Ser	
	80					85					90					
gtt	tta	atg	cat	cag	ttt	gat	gat	gcc	gtc	agt	atc	act	gtg	gca	ata	756
Val	Leu	Met	His	<b>Gl</b> n	Phe	Asp	Asp	Ala	Val	Ser	Ile	Thr	Val	Ala	Ile	
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ctt	atc	gtt	gtt	aca	gtt	gcc	ttt	gtt	cag	gaa	tat	cgt	tca	gaa	aaa	804
Leu	Ile	Val	Val	Thr	Val	Ala	Phe	Val	Gln	Glu	Tyr	Arg	Ser	Glu	Lys	
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tct	ctt	gaa	gaa	ttg	agt	aaa	ctt	gtg	cca	cca	gaa	tgc	cat	tgt	gtg	852
Ser	Leu	Glu	Glu	Leu	Ser	Lys	Leu	Val	Pro	Pro	Glu	Cys	His	Cys	Val	
			130					135					140			
cgt	gaa	gga	aaa	ttg	gag	cat	aca	ctt	gcc	cga	gac	ttg	gtt	cca	ggt	900
Arg	G1u	Gly	Lys	Leu	Glu	His	Thr	Leu	Ala	Arg	Asp	Leu	Val	Pro	Gly	
								485/	735							

V	VO 02	/0537:	37												РСТ/Л	P01/11389
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Asp	Thr	Val	Cys	Leu	Ser	Val	Gly	Asp	Arg	Val	Pro	Ala	Asp	Leu	Arg	
	160					165					170					
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Leu	Phe	G1u	Ala	Val	Asp	Leu	Ser	Ile	Asp	Glu	Ser	Ser	Leu	Thr	Gly	
175					180					185					190	
gag	aca	acg	cct	tgt	tct	aag	gtg	aca	gct	cct	cag	cca	gct	gca	act	1044
Glu	Thr	Thr	Pro	Cys	Ser	Lys	Val	Thr	Ala	Pro	Gln	Pro	Ala	Ala	Thr	
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gtc aga tgt ggc aaa gca aag ggt gtt gtc att gga aca gga gaa aat 1140 Val Arg Cys Gly Lys Ala Lys Gly Val Val Ile Gly Thr Gly Glu Asn 225 230 235

tct gaa ttt ggg gag gtt ttt aaa atg atg caa gca gaa gag gca cca 1188 Ser Glu Phe Gly Glu Val Phe Lys Met Met Gln Ala Glu Glu Ala Pro . 240 245 250

aaa acc cct ctg cag aag agc atg gac ctc tta gga aaa caa ctt tcc 1236 Lys Thr Pro Leu Gln Lys Ser Met Asp Leu Leu Gly Lys Gln Leu Ser 255 260 265 270

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Phe	Tyr	Ser	Phe	Gly	Ile	Ile	Gly	Ile	Ile	Met	Leu	Val	Gly	Trp	Leu	
				275					280					285		
ctg	gga	aaa	gat	atc	ctg	gaa	atg	ttt	act	att	agt	gta	agt	ttg	gct	1332
Leu	Gly	Lys	Asp	Ile	Leu	Glu	Met	Phe	Thr	Ile	Ser	Val	Ser	Leu	Ala	
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Val	Ala	Ala	Ile	Pro	Glu	Gly	Leu	Pro	Ile	Val	Val	Thr	Val	Thr	Leu	
		305					310					315				
gct	ctt	ggt	gtt	atg	aga	atg	gtg	aag	aaa	agg	gcc	att	gtg	aaa	aag	1428
Ala		Gly	Val	Met	Arg		Val	Lys	Lys	Arg	Ala	Ile	Val	Lys	Lys	
	320					325					330					
		att														1476
	Pro	Ile	Val	Glu		Leu	Gly	Cys	Cys		Val	He	Cys	Ser		
335					340					345					350	
	+	~~~		_+-			+		-+-	aat	~++	+		-+-	***	1504
		gga														1524
LYS	1111	Gly	1111	355	1111	Lys	ASII	GIU	360	1111	Val	1111	птѕ	365	riie	
				300					300					300		
act	tca	gat	øøt:	ctg	cat	get	gag	øt.t.	act	gga	gtt	ggc	tat	aat	caa	1572
		Asp														10.2
- ***			370					375		- <b>-</b> ,		,	380			
													_ 30			

1620

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Phe	Gly	Glu	Val	Ile	Val	Asp	Gly	Asp	Val	Val	His	Gly	Phe	Tyr	Asn	
		385					390					395				
cca	gct	gtt	agc	aga	att	gtt	gag	gcg	ggc	tgt	gtg	tgc	aat	gat	gct	1668
Pro	Ala	Val	Ser	Arg	Ile	Val	Glu	Ala	G1y	Cys	Val	Cys	Asn	Asp	Ala	
	400					405					410					
gta	att	aga	aac	aat	act	cta	atg	ggg	aag	cca	aca	gaa	ggg	gcc	tta	1716
Val	Ile	Arg	Asn	Asn	Thr	Leu	Met	Gly	Lys	Pro	Thr	Glu	Gly	Ala	Leu	
415					420					425					430	
att	gct	ctt	gca	atg	aag	atg	ggt	ctt	gat	gga	ctt	caa	caa	gac	tac	1764
Ile	Ala	Leu	Ala	Met	Lys	Met	Gly	Leu	Asp	Gly	Leu	G1n	G1n	Asp	Tyr	
				435					440					445		
atc	aga	aaa	gct	gaa	tac	cct	ttt	agc	tct	gag	caa	aag	tgg	atg	gct	1812
Ile	Arg	Lys	Ala	G1u	Tyr	Pro	Phe	Ser	Ser	Glu	Gln	Lys	Trp	Met	Ala	
			450					455					460		•	
							-									
gtt	aag	tgt	gta	cac	cga	aca	cag	cag	gac	aga	cca	gag	att	tgt	ttt	1860
Val	Lys	Cys	Val	His	Arg	Thr	Gln	G1n	Asp	Arg	Pro	G1u	Ile	Cýs	Phe	
		465					470					475				
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	480					485					490					
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Se	r Lys	Gly	GIn	Thr	Leu	Thr	Leu	Thr	Gln	GIn	GIn	Arg	Asp	Val	Tyr	
49	5				500					505					510	
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caa	a caa	gag	aag	gca	cgc	atg	ggc	tca	gcg	gga	ctc	aga	gtt	ctt	gct	2004
G1:	ı Gln	Glu	Lys	Ala	Arg	Met	Gly	Ser	Ala	Gly	Leu	Arg	Val	Leu	Ala	
				515					520					525		
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Let	ı Ala	Ser	Gly	Pro	Glu	Leu	Gly	G1n	Leu	Thr	Phe	Leu	Gly	Leu	Val	
			530					535					540			
gga	atc	att	gat	cca	cct	aga	act	ggt	gtg	aaa	gaa	gct	gtt	aca	aca	2100
G1,	7 Ile	Ile	Asp	Pro	Pro	Arg	Thr	Gly	Val	Lys	Glu	Ala	Val	Thr	Thr	
		545					550					555				
cto	att	gcc	tca	gga	gta	tca	ata	aaa	atg	att	act	gga	gat	tca	cag	2148
Let	Ile	Ala	Ser	Gly	Val	Ser	Ile	Lys	Met	Ile	Thr	Gly	Asp	Ser	Gln	
	560					565					570					
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Glu	Thr	Ala	Val	Ala	Ile	Ala	Ser	Arg	Leu	Gly	Leu	Tyr	Ser	Lys	Thr	
575	;				580					585					590	
	cag															2244
Ser	Gln	Ser	Val		Gly	G1u	G1u	Ile		Ala	Met	Asp	Val	G1n	Gln	
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															•	
_	tca				_											2292
Leu	Ser	Gln	Ile	Val	Pro	Lys	Val	Ala 489/		Phe	Tyr	Arg	Ala	Ser	Pro	
								.051								

			610					615					620			
					att Ile											2340
VIE	1112	625	Mec	Lys	116	116	630	Del	Leu	OIII	Lys	635	Oly	Der	Val	
					gat Asp											2388
vai	640	Mec	1111	Gly	nsp	645	vai	ASII	лър	ліа	650	NIG	Leu	Lys	·	
					gcg			_				-	_	_		2436
Ala 655	Asp	Ile	Gly	Val	Ala 660	Met	Gly	Gln	Thr	G1y 665	Thr	Asp	Val	Cys	Lys 670	
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Glu	Ala	Ala	Asp	Met 675	Ile	Leu	Val	Asp	Asp 680	Asp	Phe	G1n	Thr	Ile 685	Met	
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Ser	Ala	Ile	Glu 690	Glu	G1y	Lys	Gly	Ile 695	Tyr	Asn	Asn	Ile	Lys 700	Asn	Phe	
gtt	aga	ttc	cag	ctg	agc	acg	agt	ata	gca	gca	tta	act	tta	atc	tca	2580
Val	Arg	Phe 705	Gln	Leu	Ser	Thr	Ser 710	Ile	Ala	Ala	Leu	Thr 715	Leu	Ile	Ser	
†+ <i>a</i>	act		<b>+</b> †a	atσ	aac	+++		aat	cot	ctc	aat		atα	caa	2++	2628
					Asn											2020
	720					725					730					

490/735

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WO 02/053737

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735					740					745					750	
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gta	gaa	cca	gtg	gat	aaa	gat	gtc	att	cgt	aaa	cct	cct	cgc	aac	tgg	2724
Val	G1u	Pro	Val	Asp	Lys	Asp	Val	Ile	Arg	Lys	Pro	Pro	Arg	Asn	Trp	
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Lys	Asp	Ser	Ile	Leu	Thr	Lys	Asn	Leu	Ile	Leu	Lys	Ile	Leu	Val	Ser	
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Ser	Ile	Ile	Ile	Val	Cys	Gly	Thr	Leu	Phe	Val	Phe	Trp	Arg	G1u	Leu	
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cga	gac	aat	gtg	att	aca	cct	cga	gac	aca	aca	atg	acc	ttc	aca	tgc	2868
Arg	Asp	Asn	Val	Ile	Thr	Pro	Arg	Asp	Thr	Thr	Met	Thr	Phe	Thr	Cys	
	800					805					810					
ttt	gtg	ttt	ttt	gac	atg	ttc	aat	gca	cta	agt	tcc	aga	tcc	cag	acc	2916
Phe	Val	Phe	Phe	Asp	Met	Phe	Asn	Ala	Leu	Ser	Ser	Arg	Ser	Gln	Thr	
815					820					825					830	
aag	tct	gtg	ttt	gag	att	gga	ctc	tgc	agt	aat	aga	atg	ttt	tgc	tat	2964
Lys	Ser	Val	Phe	Glu	Ile	Gly	Leu	Cys	Ser	Asn	Arg	Met	Phe	Cys	Tyr	
				835					840					845		

3012

gca gtt ctt gga tcc atc atg gga caa tta cta gtt att tac ttt cct Ala Val Leu Gly Ser Ile Met Gly Gln Leu Leu Val Ile Tyr Phe Pro 850 855 860 ccg ctt cag aag gtt ttt cag act gag agc cta agc ata ctg gat ctg 3060 Pro Leu Gln Lys Val Phe Gln Thr Glu Ser Leu Ser Ile Leu Asp Leu 865 870 875 ttg ttt ctt ttg ggt ctc acc tca tca gtg tgc ata gtg gca gaa att 3108 Leu Phe Leu Leu Gly Leu Thr Ser Ser Val Cys Ile Val Ala Glu Ile 880 885 890 ata aag aag gtt gaa agg agc agg gaa aag atc cag aag cat gtt agt 3156 Ile Lys Lys Val Glu Arg Ser Arg Glu Lys Ile Gln Lys His Val Ser 895 900 905 910 tcg aca tca tca tct ttt ctt gaa gta tgatgcatat tgcattattt 3203 Ser Thr Ser Ser Ser Phe Leu Glu Val 915 tatttgcaaa ctaggaattg cagtctgagg atcatttaga agggcaagtt caagaggata 3263 tgaagatttg agaacttttt aactattcat tgactaaaaa tgaacattaa tgttaaagac 3323 ttaagacttt aacctgctgg cagtcccaaa tgaaattatg caactttgat atcatattcc 3383 ttgatttaaa ttggcttttg tgattgagtg aaactttata aagcatatgg tcagttattt 3443

aattaaaaag gcaaaacctg aaccaccttc tgcacttaaa gaagtctaac agtacaaata 3503 492/735

cactatctat cttagataga tatattttt tttatttta aatattgtac tatttatggt 3563

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3612

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<211> 382

<212> PRT

<213> Homo sapiens

<400> 135

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20 25 30

Arg Val Glu Met Glu Asp Ala His Thr Ala Val Ile Gly Leu Pro Ser
35 40 45

Gly Leu Glu Ser Trp Ser Phe Phe Ala Val Tyr Asp Gly His Ala Gly
50 55 60

Ser Gln Val Ala Lys Tyr Cys Cys Glu His Leu Leu Asp His Ile Thr
65 70 75 80

Asn Asn Gln Asp Phe Lys Gly Ser Ala Gly Ala Pro Ser Val Glu Asn

85

90

95

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Val	Lys	Asn	Gly	Ile	Arg	Thr	Gly	Phe	Leu	Glu	Ile	Asp	Glu	His	Met
			100					105					110		
Arg	Val	Met 115	Ser	Glu	Lys	Lys	His 120	Gly	Ala	Asp	Arg	Ser 125	Gly	Ser	Thr
		110					120					120			
Ala	Val	Gly	Val	Leu	Ile	Ser	Pro	Gln	His.	Thr	Tyr	Phe	Ile	Asn	Cys
	130					135					140				
G1y	Asp	Ser	Arg	Gly	Leu	Leu	Cys	Arg	Asn	Arg	Lys	Val	His	Phe	Phe
145					150					155					160
Thr	Gln	Asp	His	Lys	Pro	Ser	Asn	Pro	Leu	Glu	Lys	Glu	Arg	Ile	Gln
				165					170					175	
Asn	Ala	Gly	G1y	Ser	Val	Met	Ile	Gln	Arg	Val	Asn	Gly	Ser	Leu	Ala
			180					185					190		
Vo1	Som	Λ <b></b>	410	Lou	C1	Aan	Dho	Aan	Т	Ia	C···a	V-1	u: a	C1	T ci
vaı	ser	195	міа	Leu	GIA	ASP	200	Asp	lyr	Lys	cys	205	nis	GIY	Lys
Gly		Thr	Glu	Gln	Leu		Ser	Pro	Glu	Pro		Val	His	Asp	Ile
	210					215					220				
Glu	Arg	Ser	Glu	Glu	Asp	Asp	Gln	Phe	Ile	Ile	Leu	Ala	Cys	Asp	G1y
225					230					235					240
Ile	Trp	Asp	Val	Met	G1y	Asn	Glu	Glu 494/		Cys	Asp	Phe	Val	Arg	Ser
								,							

245 250 255

Arg Leu Glu Val Thr Asp Asp Leu Glu Lys Val Cys Asn Glu Val Val
260 265 270

Asp Thr Cys Leu Tyr Lys Gly Ser Arg Asp Asn Met Ser Val Ile Leu 275 280 285

Ile Cys Phe Pro Asn Ala Pro Lys Val Ser Pro Glu Ala Val Lys Lys 290 295 300

Glu Ala Glu Leu Asp Lys Tyr Leu Glu Cys Arg Val Glu Glu Ile Ile 305 310 315 320

Lys Lys Gln Gly Glu Gly Val Pro Asp Leu Val His Val Met Arg Thr
325 330 335

Leu Ala Ser Glu Asn Ile Pro Ser Leu Pro Pro Gly Gly Glu Leu Ala 340 345 350

Ser Lys Arg Asn Val Ile Glu Ala Val Tyr Asn Arg Leu Asn Pro Tyr 355 360 365

Lys Asn Asp Asp Thr Asp Ser Thr Ser Thr Asp Asp Met Trp
370 375 380

<210> 136

<211> 2467

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (444).. (1589)

<400> 136

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cgggteetea ggeggetgtt geteeggaac gggtggttgg ggagggggg gtggggggac 120

tetagacage tgaggegga aagegatgag teeteggete tteeteetee tteteegga 180

cccgetetet geeteetet ccaacgeeg gatgatetga geeggaggg egeegacage 240

cggggggeeeg gaegeagee ggeteetee eteeteegee eetteeegg 300

cccgeegetg eageggtgae eetteeeeg getgeegeeg tegeegeege ggtgaeeeee 360

teeeeggetg eegeegeege egeeteegee gaecagggae etgeegeege ggtgaeeeee 420

cggacetaga ggateaagae ata atg gga gea ttt tta gae aag eea aag atg 473

Met Gly Ala Phe Leu Asp Lys Pro Lys Met

1 5 10

gaa aag cat aat gcc cag ggg cag ggt aat ggg ttg cga tat ggg cta 521 Glu Lys His Asn Ala Gln Gly Gln Gly Asn Gly Leu Arg Tyr Gly Leu

> 15 20 25 496/735

agc	agc	atg	caa	ggc	tgg	cgt	gtt	gaa	atg	gag	gat	gca	cat	acg	gct	569
Ser	Ser	Met	Gln	Gly	Trp	Arg	Val	Glu	Met	Glu	Asp	Ala	His	Thr	Ala	
			30					35					40			
gtg	atc	ggt	ttg	cca	agt	gga	ctt	gaa	tcg	tgg	tca	ttc	ttt	gct	gtg	617
Val	Ile	Gly	Leu	Pro	Ser	Gly	Leu	Glu	Ser	Trp	Ser	Phe	Phe	Ala	Val	
		45					50					55				
tat	gat	ggg	cat	gct	ggt	tct	cag	gtt	gcc	aaa	tac	tgc	tgt	gag	cat	665
Tyr	Asp	Gly	His	Ala	Gly	Ser	Gln	Val	Ala	Lys	Tyr	Cys	Cys	Glu	His	
	60					65					70					
ttg	tta	gat	cac	atc	acc	aat	aac	cag	gat	ttt	aaa	ggg	tct	gca	gga	713
Leu	Leu	Asp	His	Ile	Thr	Asn	Asn	Gln	Asp	Phe	Lys	Gly	Ser	Ala	Gly	
75					80					85					90	
gca	cct	tct	gtg	gaa	aat	gta	aag	aat	gga	atc	aga	aca	ggt	ttt	ctg	761
Ala	Pro	Ser	Val	Glu	Asn	Val	Lys	Asn	Gly	Ile	Arg	Thr	Gly	Phe	Leu	
				95					100					105		
gag	att	gat	gaa	cac	atg	aga	gtt	atg	tca	gag	aag	aaa	cat	ggt	gca	809
Glu	Ile	Asp	Glu	His	Met	Arg	Val	Met	Ser	G1u	Lys	Lys	His	Gly	Ala	
			110					115					120			
gat	aga	agt	ggg	tca	aca	gct	gta	ggt	gtc	tta	att	tct	ccc	caa	cat	857
Asp	Arg	Ser	Gly	Ser	Thr	Ala	Va1	Gly	Val	Leu	Ile	Ser	Pro	Gln	His	
		125					130					135				

act	tat	ttc	att	aac	tgt	gga	gac	tca	aga	ggt	tta	ctt	tgt	agg	aac	905
Thr	Tyr	Phe	Ile	Asn	Cys	Gly	Asp	Ser	Arg	Gly	Leu	Leu	Cys	Arg	Asn	
	140					145					150					
agg	aaa	gtt	cat	ttc	ttc	aca	caa	gat	cac	aaa	cca	agt	aat	ccg	ctg	953
Arg	Lys	Val	His	Phe	Phe	Thr	Gln	Asp	His	Lys	Pro	Ser	Asn	Pro	Leu	
155					160					165					170	
gag	aaa	gaa	cga	att	cag	aat	gca	ggt	ggc	tct	gta	atg	att	cag	cgt	1001
Glu	Lys	Glu	Arg	Ile	Gln	Asn	Ala	Gly	Gly	Ser	Val	Met	Ile	Gln	Arg	
				175					180					185		
gtg	aat	ggc	tct	ctg	gct	gta	tcg	agg	gcc	ctt	ggg	gat	ttt	gat	tac	1049
Val	Asn	G1y	Ser	Leu	Ala	Val	Ser	Arg	Ala	Leu	Gly	Asp	Phe	Asp	Tyr	
			190	•				195					200			
aaa	tgt	gtc	cat	gga	aaa	ggt	cct	act	gag	cag	ctt	gtc	tca	cca	gag	1097
Lys	Cys	Val	His	Gly	Lys	Gly	Pro	Thr	G1u	G1n	Leu	Val	Ser	Pro	Glu	
		205					210					215				
cct	gaa	gtc	cat	gat	att	gaa	aga	tct	gaa	gaa	gat	gat	cag	ttc	att	1145
Pro	Glu	Val	His	Asp	Ile	Glu	Arg	Ser	Glu	Glu	Asp	Asp	Gln	Phe	Ile	
	220					225					230					
atc	ctt	gca	tgt	gat	ggt	atc	tgg	gat	gtt	atg	gga	aat	gaa	gag	ctc	1193
Ile	Leu	Ala	Cys	Asp	G1y	Ile	Trp	Asp	Val	Met	Gly	Asn	Glu	Glu	Leu	
235					240					245					250	
tgt	gat	ttt	gta	aga	tcc	aga	ctt	gaa	gtc	act	gat	gac	ctt	gag	aaa	1241
								498/	735							

Cys	Asp	Phe	Val	Arg	Ser	Arg	Leu	Glu	Val	Thr	Asp	Asp	Leu	Glu	Lys	
				255					260					265		
gtt	tgc	aat	gaa	gta	gtc	gac	acc	tgt	ttg	tat	aag	gga	agt	cga	gac	1289
Val	Cys	Asn	Glu	Val	Val	Asp	Thr	Cys	Leu	Tyr	Lys	Gly	Ser	Arg	Asp	
			270					275					280			
aac	atg	agt	gtg	att	ttg	atc	tgt	ttt	cca	aat	gca	ссс	aaa	gta	tcg	1337
Asn	Met	Ser	Val	Ile	Leu	Ile	Cys	Phe	Pro	Asn	Ala	Pro	Lys	Val	Ser	
		285					290		•			295				
cca	gaa	gca	gtg	aag	aag	gag	gca	gag	ttg	gac	aag	tac	ctg	gaa	tgc	1385
Pro	Glu	Ala	Val	Lys	Lys	Glu	Ala	Glu	Leu	Asp	Lys	Tyr	Leu	Glu	Cys	
	300					305					310					
aga	gta	gaa	gaa	atc	ata	aag	aag	cag	ggg	gaa	ggc	gtc	ссс	gac	tta	1433
Arg	Va1	G1u	Glu	Ile	Ile	Lys	Lys	Gln	Gly	Glu	Gly	Val	Pro	Asp	Leu	
315					320					325					330	
gtc	cat	gtg	atg	cgc	aca	tta	gcg	agt	gag	aac	atc	ccc	agc	ctc	cca	1481
Val	His	Val	Met	Arg	Thr	Leu	Ala	Ser	Glu	Asn	Ile	Pro	Ser	Leu	Pro	
				335					340					345		
cca	ggg	ggt	gaa	ttg	gca	agc	aag	agg	aat	gtt	att	gaa	gcc	gtt	tac	1529
Pro	Gly	Gly	Glu	Leu	Ala	Ser	Lys	Arg	Asn	Val	Ile	Glu	Ala	Val	Tyr	
			350					355					360			
aat	aga	ctg	aat	cct	tac	aaa	aat	gac	gac	act	gac	tct	aca	tca	aca	1577
Asn	Arg	Leu	Asn	Pro	Tyr	Lys	Asn	Asp	Asp	Thr	Asp	Ser	Thr	Ser	Thr	
								499	735							

365 370 375

gat gat atg tgg taaaactgct catctagcca tggagtttac cttcacctcc 1629
Asp Asp Met Trp

380

aaaggagagt acagctcaac tttgttgaaa cttttaacat ccatcctcaa ctttaaggaa 1689 ggggatatga catgggtgag aatgattaca tcagagaact tcagcagtac aacagctagc 1749 ccagaactga ttttttttt ttttttgtaa atttgagact tatgtaagcg tgatttcaaa 1809 ccataattcg tgttgtaaat cagactccag caatttttgt tgtatgattt tgtttttttg 1869 taaagtgtaa ttgtccttgt acaaaatgct catatttaat tatgaactgc tttaaatcac 1929 tatcaaagtt acaagaaatg tttggcttat tgtgtgatgc aacagatata tagccctttc 1989 aagtcatgtt gtgtttggac ttggggttgg aacagggaga gcagcagcca tgtcagctac 2049 acgctcaaat gtgcagatga ttatggaaaa taacctcaaa atcttacaaa gctgaacatc 2109 caaggagtta ttgaaaacta tcttaaatgt tcttggtagg ggagttggca ttgttgataa 2169 agccagtccc ttcatttaac tgtctttcag gatgttcctt cgttgtttcc atgagtattg 2229 caggtaataa tacagtgtat tcataagaat ctcaatcttg gggctaaatg ccttgtttct 2289 ttgcacctct tttcaagtcc ttacatttaa ttactaattg ataagcagca gcttcctaca 2349 500/735

tatagtagga aactgccaca tttttgctat catgattggc tgggcctgct gctgttccta 2409

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<210> 137

<211> 358

<212> PRT

<213> Homo sapiens

<400> 137

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Thr Ile Lys Tyr Lys Asp Glu Asp Gly Asp Leu Ile Thr Ile Phe Asp
20 25 30

Ser Ser Asp Leu Ser Phe Ala Ile Gln Cys Ser Arg Ile Leu Lys Leu
35 40 45

Thr Leu Phe Val Asn Gly Gln Pro Arg Pro Leu Glu Ser Ser Gln Val
50 55 60

Lys Tyr Leu Arg Arg Glu Leu Ile Glu Leu Arg Asn Lys Val Asn Arg 65 70 75 80

Leu Leu Asp Ser Leu Glu Pro Pro Gly Glu Pro Gly Pro Ser Thr Asn

85

90

95

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Ile	Pro	Glu	Asn	Asp	Thr	Val	Asp	Gly	Arg	G1u	G1u	Lys	Ser	Ala	Ser
			100					105					110		•
Asp	Ser	Ser	Gly	Lys	Gln	Ser	Thr	G1n	Val	Met	Ala	Ala	Ser	Met	Ser
		115					120					125			
Ala	Phe	Asp	Pro	Leu	Lys	Asn	G1n	Asp	Glu	Ile	Asn	Lys	Asn	Val	Met
	130					135					140				
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	Ala	Phe	Gly	Leu		Asp	Asp	Gln	Val		Gly	Pro	Pro	Ser	
145					150					155					160
D	47.	C1	A	<b>A</b>	C	C1	T1	D	<b>A</b>	C	T1 -	A 1 -	C	C	C
Pro	Ala	Glu	Asp		Ser	СТА	ınr	Pro		Ser	TIE	Ala	ser	Ser	Ser
				165					170					175	-
Ser	Ala	Ala	His	Pro	Pro	Glv	Val	Gln	Pro	G1n	Gl n	Pro	Pro	Tyr	Thr
			180			,		185					190	-,-	
Gly	Ala	G1n	Thr	Gln	Ala	Gly	G1n	Met	Tyr	G1n	Gln	Tyr	Gln	G1n	Gln
		195					200					205			
Ala	Gly	Tyr	Gly	Ala	G1n	G1n	Pro	Gln	Ala	Pro	Pro	Gln	Gln	Pro	Gln
	210					215					220				
Gln	Tyr	Gly	Ile	Gln	Tyr	Ser	Ala	Ser	Tyr	Ser	Gln	Gln	Thr	Gly	Pro
225					230					235					240
Gln	Gln	Pro	Gln	Gln	Phe	G1n	Gly	Tyr	Gly	Gln	Gln	Pro	Thr	Ser	Gln

502/735

1

245 250 255

Ala Pro Ala Pro Ala Phe Ser Gly Gln Pro Gln Gln Leu Pro Ala Gln 260 265 270

Pro Pro Gln Gln Tyr Gln Ala Ser Asn Tyr Pro Ala Gln Thr Tyr Thr
275 280 285

Ala Gln Thr Ser Gln Pro Thr Asn Tyr Thr Val Ala Pro Ala Ser Gln 290 295 300

Pro Gly Met Ala Pro Ser Gln Pro Gly Ala Tyr Gln Pro Arg Pro Gly 305 310 315 320

Phe Thr Ser Leu Pro Gly Ser Thr Met Thr Pro Pro Pro Ser Gly Pro 325 330 335

Asn Pro Tyr Ala Arg Asn Arg Pro Pro Phe Gly Gln Gly Tyr Thr Gln 340 345 350

Pro Gly Pro Gly Tyr Arg 355

<210> 138

<211> 1519

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (11).. (1084)

<400> 138

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1 5 10

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Asp Glu Val Thr Ile Lys Tyr Lys Asp Glu Asp Gly Asp Leu Ile Thr
15 20 25

att ttt gat agt tct gac ctt tcc ttt gca att cag tgc agt agg ata 145

Ile Phe Asp Ser Ser Asp Leu Ser Phe Ala Ile Gln Cys Ser Arg Ile

30 35 40 45

ctg aaa ctg aca tta ttt gtt aat ggc cag cca aga ccc ctt gaa tca 193
Leu Lys Leu Thr Leu Phe Val Asn Gly Gln Pro Arg Pro Leu Glu Ser
50 55 60

agt cag gtg aaa tat ctc cgt cga gaa ctg ata gaa ctt cga aat aaa 241 Ser Gln Val Lys Tyr Leu Arg Arg Glu Leu Ile Glu Leu Arg Asn Lys 65 70 75

gtg aat cgt tta ttg gat agc ttg gaa cca cct gga gaa cca gga cct 289
Val Asn Arg Leu Leu Asp Ser Leu Glu Pro Pro Gly Glu Pro Gly Pro
80 85 90

tcc	acc	aat	att	cct	gaa	aat	gat	act	gtg	gat	ggt	agg	gaa	gaa	aag	337
Ser	Thr	Asn	Ile	Pro	Glu	Asn	Asp	Thr	Val	Asp	Gly	Arg	Glu	Glu	Lys	
	95					100					105					
tct	gct	tct	gat	tct	tct	gga	aaa	cag	tct	act	cag	gtt	atg	gca	gca	385
Ser	Ala	Ser	Asp	Ser	Ser	Gly	Lys	G1n	Ser	Thr	Gln	Val	Met	Ala	Ala	
110					115					120					125	
agt	atg	tct	gct	ttt	gat	cct	tta	aaa	aac	caa	gat	gaa	atc	aat	aaa	433
Ser	Met	Ser	Ala	Phe	Asp	Pro	Leu	Lys	Asn	G1n	Asp	Glu	Ile	Asn	Lys	
				130					135					140		
aat	gtt	atg	tca	gcg	ttt	ggc	tta	aca	gat	gat	cag	gtt	tca	ggg	cca	481
Asn	Val	Met	Ser	Ala	Phe	Gly	Leu	Thr	Asp	Asp	Gln	Val	Ser	Gly	Pro	
			145					150					155			
ссс	agt	gct	cct	gca	gaa	gat	cgt	tca	gga	aca	ccc	gac	agc	att	gct	529
Pro	Ser	Ala	Pro	Ala	Glu	Asp	Arg	Ser	Gly	Thr	Pro	Asp	Ser	Ile	Ala	
		160					165					170				
tcc	tcc	tcc	tca	gca	gct	cac	cca	cca	ggc	gtt	cag	cca	cag	cag	cca	577
Ser	Ser	Ser	Ser	Ala	Ala	His	Pro	Pro	G1y	Val	Gln	Pro	G1n	G1n	Pro	
	175					180					185					
cca	tat	aca	gga	gct	cag	act	caa	gca	ggt	cag	atg	tac	caa	cag	tac	625
Pro	Tyr	Thr	Gly	Ala	Gln	Thr	Gln	Ala	Gly	Gln	Met	Tyr	G1n	Gln	Tyr	
190					195					200					205	
cag	caa	cag	gcc	ggc	tat	ggt	gca	cag	cag	ccg	cag	gct	cca	cct	cag	673
								505/	735							

Gln	Gln	Gln	Ala	Gly	Tyr	Gly	Ala	Gln	G1n	Pro	Gln	Ala	Pro	Pro	G1n	
				210					215					220		
cag	cct	caa	cag	tat	ggt	att	cag	tat	tca	gca	agc	tat	agt	cag	cag	721
Gln	Pro	Gln	Gln	Tyr	Gly	Ile	Gln	Tyr	Ser	Ala	Ser	Tyr	Ser	Gln	G1n	
			225					230					235			
act	gga	ccc	caa	caa	cct	cag	cag	ttc	cag	gga	tat	ggc	cag	caa	cca	769
Thr	Gly	Pro	G1n	Gln	Pro	Gln	Gln	Phe	Gln	Gly	Tyr	Gly	Gln	Gln	Pro	
		240					245					250				
act	tcc	cag	gca	cca	gct	cct	gcc	ttt	tct	ggt	cag	cct	caa	caa	ctg	817
Thr	Şer	Gln	Ala	Pro	Ala	Pro	Ala	Phe	Ser	Gly	G1n	Pro	Gln	Gln	Leu	
	255					260					265					
cct	gct	cag	ccg	cca	cag	cag	tac	cag	gcg	agc	aat	tat	cct	gca	caa	865
Pro	Ala	Gln	Pro	Pro	Gln	G1n	Tyr	G1n	Ala	Ser	Asn	Tyr	Pro	Ala	Gln	
270					275					280					285	
act	tac	act	gcc	caa	act	tct	cag	cct	act	aat	tat	act	gtg	gct	cct	913
Thr	Tyr	Thr	Ala	Gln	Thr	Ser	G1n	Pro	Thr	Asn	Tyr	Thr	Val	Ala	Pro	
				290					295					300		
gcc	tct	caa	cct	gga	atg	gct	cca	agc	caa	cct	ggg	gcc	tat	caa	cca	961
Ala	Ser	Gln	Pro	Gly	Met	Ala	Pro	Ser	Gln	Pro	Gly	Ala	Tyr	G1n	Pro	
			305			•		310					315			
aga	cca	ggt	ttt	act	tca	ctt	cct	gga	agt	acc	atg	acc	cct	cct	cca	1009
Arg	Pro	Gly	Phe	Thr	Ser	Leu	Pro	Gly	Ser	Thr	Met	Thr	Pro	Pro	Pro	
								506/	735							

320 325 330

agt ggg cct aat cct tat gcg cgt aac cgt cct ccc ttt ggt cag ggc 1057

Ser Gly Pro Asn Pro Tyr Ala Arg Asn Arg Pro Pro Phe Gly Gln Gly

335 340 345

tat acc caa cct gga cct ggt tat cga taaggagget cctctacacc . 1104

Tyr Thr Gln Pro Gly Pro Gly Tyr Arg

350 355

aattaatgta getgetaget attggeetee caaaagaete cagtactatt ttaatttgta 1164

ttgaagaagt teagaaattt aaaageagag catttttat gatateattg ttggtgttaa 1224

ttgaaagtat aatttgetgg aacacaaaga ceaaaatgaa agtttttee teeetgetta 1284

aaaatgtage agettettag ttaetttgga acactactet taeatgtata aagtgattga 1344

ettgaettte tagetteeet tgteeggagg atattaaaat getagggtga ggtttageea 1404

tettaettgg ettttaeta ttaacatgat gtaetaaagt agageeettt gagaatacaa 1464

gatattatgt ataaaatgta acactgatga taggttaata aagatgattg aatee 1519

<210> 139

<211> 396

<212> PRT

<213> Homo sapiens

<400> 139

Met Asn Gly Gln Leu Asp Leu Ser Gly Lys Leu Ile Val Lys Ala Gln

1 5 10 15

Leu Gly Glu Asp Ile Arg Arg Ile Pro Ile His Asn Glu Asp Ile Thr
20 25 30

Tyr Asp Glu Leu Val Leu Met Met Gln Arg Val Phe Arg Gly Lys Leu
35 40 45

Leu Ser Asn Asp Glu Val Thr Ile Lys Tyr Lys Asp Glu Asp Gly Asp
50 55 60

Leu Ile Thr Ile Phe Asp Ser Ser Asp Leu Ser Phe Ala Ile Gln Cys
65 70 75 80

Ser Arg Ile Leu Lys Leu Thr Leu Phe Val Asn Gly Gln Pro Arg Pro
85 90 95

Leu Glu Ser Ser Gln Val Lys Tyr Leu Arg Arg Glu Leu Ile Glu Leu
100 105 110

Arg Asn Lys Val Asn Arg Leu Leu Asp Ser Leu Glu Pro Pro Gly Glu 115 120 125

Pro Gly Pro Ser Thr Asn Ile Pro Glu Asn Asp Thr Val Asp Gly Arg
130 135 140

170

175

165

Ile Asn Lys Asn Val Met Ser Ala Phe Gly Leu Thr Asp Asp Gln Val 180 185 190

Ser Gly Pro Pro Ser Ala Pro Ala Glu Asp Arg Ser Gly Thr Pro Asp 195 200 205

Ser Ile Ala Ser Ser Ser Ser Ala Ala His Pro Pro Gly Val Gln Pro 210 215 220

Gln Gln Pro Pro Tyr Thr Gly Ala Gln Thr Gln Ala Gly Gln Met Tyr 225 230 235 240

Gln Gln Tyr Gln Gln Gln Ala Gly Tyr Gly Ala Gln Gln Pro Gln Ala
245 250 255

Pro Pro Gln Gln Pro Gln Gln Tyr Gly Ile Gln Tyr Ser Ala Ser Tyr
260 265 270

Ser Gln Gln Thr Gly Pro Gln Gln Pro Gln Gln Phe Gln Gly Tyr Gly
275 280 285

Gln Gln Pro Thr Ser Gln Ala Pro Ala Pro Ala Phe Ser Gly Gln Pro
290 295 300
509/735

Gln Gln Leu Pro Ala Gln Pro Pro Gln Gln Tyr Gln Ala Ser Asn Tyr 305 310 315 320

Pro Ala Gln Thr Tyr Thr Ala Gln Thr Ser Gln Pro Thr Asn Tyr Thr
325 330 335

Val Ala Pro Ala Ser Gln Pro Gly Met Ala Pro Ser Gln Pro Gly Ala 340 345 350

Tyr Gln Pro Arg Pro Gly Phe Thr Ser Leu Pro Gly Ser Thr Met Thr
355 360 365

Pro Pro Pro Ser Gly Pro Asn Pro Tyr Ala Arg Asn Arg Pro Pro Phe 370 375 380

Gly Gln Gly Tyr Thr Gln Pro Gly Pro Gly Tyr Arg 385 390 395

<210> 140

<211> 1641

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (19).. (1206)

<b>\400/ 140</b>	<40	<0>	140
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		1				5					10		

atc gtc aaa gct caa ctt ggg gag gat att cgg cga att cct att cat 99

Ile Val Lys Ala Gln Leu Gly Glu Asp Ile Arg Arg Ile Pro Ile His

15 20 25

aat gaa gat att act tat gat gaa tta gtg cta atg atg caa cga gtt 147
Asn Glu Asp Ile Thr Tyr Asp Glu Leu Val Leu Met Met Gln Arg Val
30 35 40

ttc aga gga aaa ctt ctg agt aat gat gaa gta aca ata aag tat aaa 195
Phe Arg Gly Lys Leu Leu Ser Asn Asp Glu Val Thr Ile Lys Tyr Lys
45 50 55

gat gaa gat gga gat ctt ata aca att ttt gat agt tct gac ctt tcc 243
Asp Glu Asp Gly Asp Leu Ile Thr Ile Phe Asp Ser Ser Asp Leu Ser
60 65 70 75

ttt gca att cag tgc agt agg ata ctg aaa ctg aca tta ttt gtt aat 291
Phe Ala Ile Gln Cys Ser Arg Ile Leu Lys Leu Thr Leu Phe Val Asn
80 85 90

ggc cag cca aga ccc ctt gaa tca agt cag gtg aaa tat ctc cgt cga 339
Gly Gln Pro Arg Pro Leu Glu Ser Ser Gln Val Lys Tyr Leu Arg Arg
95 100 105

WO 02/053737	PCT/JP01/1138

gaa	ctg	ata	gaa	ctt	cga	aat	aaa	gtg	aat	cgt	tta	ttg	gat	agc	ttg	387
Glu	Leu	Ile	Glu	Leu	Arg	Asn	Lys	Val	Asn	Arg	Leu	Leu	Asp	Ser	Leu	
		110					115					120				
gaa	cca	cct	gga	gaa	cca	gga	cct	tcc	acc	aat	att	cct	gaa	aat	gat	435
G1u	Pro	Pro	Gly	Glu	Pro	Gly	Pro	Ser	Thr	Asn	Ile	Pro	Glu	Asn	Asp	
	125					130					135					
act	gtg	gat	ggt	agg	gaa	gaa	aag	tct	gct	tct	gat	tct	tct	gga	aaa	483
Thr	Val	Asp	Gly	Arg	Glu	Glu	Lys	Ser	Ala	Ser	Asp	Ser	Ser	Gly	Lys	
140					145					150					155	
cag	tct	act	cag	gtt	atg	gca	gca	agt	atg	tct	gct	ttt	gat	cct	tta	531
Gln	Ser	Thr	G1n	Val	Met	Ala	Ala	Ser	Met	Ser	Ala	Phe	Asp	Pro	Leu	
				160					165					170		
aaa	aac	caa	gat	gaa	atc	aat	aaa	aat	gtt	atg	tca	gcg	ttt	ggc	tta	579
Lys	Asn	Gln		Glu	Ile	Asn	Lys	Asn	Val	Met	Ser	Ala	Phe	Gly	Leu	
			175					180					185			
								ccc								627
Thr	Asp		Gln	Val	Ser	Gly		Pro	Ser	Ala	Pro		Glu	Asp	Arg	
		190					195					200				
								tcc								675
Ser		Thr	Pro	Asp			Ala	Ser	Ser	Ser		Ala	Ala	His	Pro	
	205					210					215					
									1.		_					
cca	ggc	gtt	cag	cca	cag	cag	cca	cca 512/		aca	gga	gct	cag	act	caa	723

Pro	Gly	Val	Gln	Pro	Gln	G1n	Pro	Pro	Tyr	Thr	Gly	Ala	Gln	Thr	Gln	
220					225					230					235	
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Ala	Gly	Gln	Met	Tyr	G1n	G1n	Tyr	Gln	Gln	Gln	Ala	Gly	Tyr	Gly	Ala	
				240					245					250		
cag	cag	ccg	cag	gct	cca	cct	cag	cag	cct	caa	cag	tat	ggt	att	cag	819
G1n	G1n	Pro	Gln	Ala	Pro	Pro	Gln	Gln	Pro	Gln	Gln	Tyr	Gly	Ile	Gln	
			255					260					265			
tat	tca	gca	agc	tat	agt	cag	cag	act	gga	ccc	caa	caa	cct	cag	cag	867
Tyr	Ser	Ala	Ser	Tyr	Ser	G1n	Gln	Thr	Gly	Pro	Gln	Gln	Pro	G1n	G1n	
		270					275					280				
ttc	cag	gga	tat	ggc	cag	caa	cca	act	tcc	cag	gca	cca	gct	cct	gcc .	915
Phe	Gln	Gly	Tyr	G1y	G1n	Gln	Pro	Thr	Ser	G1n	Ala	Pro	Ala	Pro	Ala	
	285					290					295					
ttt	tct	ggt	cag	cct	caa	caa	ctg	cct	gct	cag	ccg	cca	cag	cag	tac	963
Phe	Ser	Gly	Gln	Pro	Gln	Gln	Leu	Pro	Ala	Gln	Pro	Pro	Gln	Gln	Tyr	
300					305					310					315	
cag	gcg	agc	aat	tat	cct	gca	caa	act	tac	act	gcc	caa	act	tct	cag	1011
Gln	Ala	Ser	Asn	Tyr	Pro	Ala	Gln	Thr	Tyr	Thr	Ala	Gln	Thr	Ser	G1n	
				320					325					330		
															•	
cct	act	aat	tat	act	gtg	gct	cct	gcc	tct	caa	cct	gga	atg	gct	cca	1059
Pro	Thr	Asn	Tyr	Thr	Val	Ala	Pro	Ala	Ser	Gln	Pro	Gly	Met	Ala	Pro	
								513	735							

335 340 345 age caa cet ggg gee tat caa eea aga eea ggt ttt act tea ett eet Ser Gln Pro Gly Ala Tyr Gln Pro Arg Pro Gly Phe Thr Ser Leu Pro 350 355 360 gga agt acc atg acc cct cct cca agt ggg cct aat cct tat gcg cgt 1155 Gly Ser Thr Met Thr Pro Pro Pro Ser Gly Pro Asn Pro Tyr Ala Arg 370 375 365 aac cgt cct ccc ttt ggt cag ggc tat acc caa cct gga cct ggt tat 1203 Asn Arg Pro Pro Phe Gly Gln Gly Tyr Thr Gln Pro Gly Pro Gly Tyr 380 385 390 395 cga taaggagget cetetacace aattaatgta getgetaget attggeetee 1256 Arg caaaagactc cagtactatt ttaatttgta ttgaagaagt tcagaaattt aaaagcagag 1316 cattttttat gatatcattg ttggtgttaa ttgaaagtat aatttgctgg aacacaaaga 1376 ccaaaatgaa agtttttcc tcctgctta aaaatgtagc agcttcttag ttactttgga 1436 acactactct tacatgtata aagtgattga cttgactttc tagcttccct tgtccggagg 1496 atattaaaat gctagggtga ggtttagcca tcttacttgg ctttttacta ttaacatgat 1556

PCT/JP01/11389

WO 02/053737

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1641

<210> 141

<211> 323

<212> PRT

<213> Homo sapiens

<400> 141

Met Ala Phe Ser Gly Ser Gln Ala Pro Tyr Leu Ser Pro Ala Val Pro 1

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Phe Ser Gly Thr Ile Gln Gly Gly Leu Gln Asp Gly Leu Gln Ile Thr

20 25 30

Val Asn Gly Thr Val Leu Ser Ser Ser Gly Thr Arg Phe Ala Val Asn

35 40 45

Phe Gln Thr Gly Phe Ser Gly Asn Asp Ile Ala Phe His Phe Asn Pro

50 55 60

Arg Phe Glu Asp Gly Gly Tyr Val Val Cys Asn Thr Arg Gln Asn Gly

65 70 75 80

Ser Trp Gly Pro Glu Glu Arg Lys Thr His Met Pro Phe Gln Lys Gly

85 90 95

Met Pro Phe Asp Leu Cys Phe Leu Val Gln Ser Ser Asp Phe Lys Val

100 105 110

Met	Val	Asn	Gly	Ile	Leu	Phe	Val	G1n	Tyr	Phe	His	Arg	Val	Pro	Phe
		115					120					125			
His	Arg	Val	Asp	Thr	Ile	Ser	Val	Asn	Gly	Ser	Val	Gln	Leu	Ser	Tyr
	130					135					140				
Ile	Ser	Phe	Gln	Pro	Pro	Gly	Val	Trp	Pro	Ala	Asn	Pro	Ala	Pro	Ile
145					150					155					160
										•					
Thr	Gln	Thr	Val	Ile	His	Thr	Val	Gln	Ser	Ala	Pro	Gly	Gln	Met	Phe
				165					170					175	
Ser	Thr	Pro	Ala	Ile	Pro	Pro	Met	Met	Tyr	Pro	His	Pro	Ala	Tyr	Pro
			180					185					190		
Met	Pro	Phe	Ile	Thr	Thr	Ile	Leu	Gly	Gly	Leu	Tyr	Pro	Ser	Lys	Ser
		195					200					205			
Ile	Leu	Leu	Ser	G1y	Thr	Val	Leu	Pro	Ser	Ala	Gln	Arg	Phe	His	Ile
	210					215					220				
Asn	Leu	Cys	Ser	Gly	Asn	His	Ile	Ala	Phe	His	Leu	Asn	Pro	Arg	Phe
225					230					235					240
Asp	Glu	Asn	Ala	Val	Val	Arg	Asn	Thr	G1n	Ile	Asp	Asn	Ser	Trp	Gly
				245					250					255	

Ser Glu Glu Arg Ser Leu Pro Arg Lys Met Pro Phe Val Arg Gly Gln 516/735

260 265 270

Ser Phe Ser Val Trp Ile Leu Cys Glu Ala His Cys Leu Lys Val Ala 275 280 285

Val Asp Gly Gln His Leu Phe Glu Tyr Tyr His Arg Leu Arg Asn Leu 290 295 300

Pro Thr Ile Asn Arg Leu Glu Val Gly Gly Asp Ile Gln Leu Thr His 305 310 315 320

Val Gln Thr

⟨210⟩ 142

<211> 1616

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

⟨222⟩ (72).. (1040)

<400> 142

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gcggcggaga g atg gcc ttc agc ggt tcc cag gct ccc tac ctg agt cca 110

Met Ala Phe Ser Gly Ser Gln Ala Pro Tyr Leu Ser Pro
517/735

1 5 10

gct gtc ccc ttt tct ggg act att caa gga ggt ctc cag gac gga ctt 158

Ala Val Pro Phe Ser Gly Thr Ile Gln Gly Gly Leu Gln Asp Gly Leu

15 20 25

cag atc act gtc aat ggg acc gtt ctc agc tcc agt gga acc agg ttt 206
Gln Ile Thr Val Asn Gly Thr Val Leu Ser Ser Ser Gly Thr Arg Phe
30 35 40 45

gct gtg aac ttt cag act ggc ttc agt gga aat gac att gcc ttc cac 254
Ala Val Asn Phe Gln Thr Gly Phe Ser Gly Asn Asp Ile Ala Phe His
50 55 60

ttc aac cct cgg ttt gaa gat gga ggg tac gtg gtg tgc aac acg agg 302
Phe Asn Pro Arg Phe Glu Asp Gly Gly Tyr Val Val Cys Asn Thr Arg
65 70 75

cag aac gga agc tgg ggg ccc gag gag agg aag aca cac atg cct ttc 350

Gln Asn Gly Ser Trp Gly Pro Glu Glu Arg Lys Thr His Met Pro Phe

80 85 90

cag aag ggg atg ccc ttt gac ctc tgc ttc ctg gtg cag agc tca gat 398

Gln Lys Gly Met Pro Phe Asp Leu Cys Phe Leu Val Gln Ser Ser Asp

95 100 105

ttc aag gtg atg gtg aac ggg atc ctc ttc gtg cag tac ttc cac cgc 446

Phe Lys Val Met Val Asn Gly Ile Leu Phe Val Gln Tyr Phe His Arg

110 125 120 125

518/735

gtg	ccc	ttc	cac	cgt	gtg	gac	acc	atc	tcc	gtc	aat	ggc	tct	gtg	cag	494
Val	Pro	Phe	His	Arg	Val	Asp	Thr	Ile	Ser	Val	Asn	Gly	Ser	Val	Gln	
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ctg	tcc	tac	atc	agc	ttc	cag	cct	ссс	ggc	gtg	tgg	cct	gcc	aac	ccg	542
Leu	Ser	Tyr	Ile	Ser	Phe	G1n	Pro	Pro	Gly	Val	Trp	Pro	Ala	Asn	Pro	
			145					150					155			
gct	ссс	att	acc	cag	aca	gtc	atc	cac	aca	gtg	cag	agc	gcc	cct	gga	590
Ala	Pro	Ile	Thr	G1n	Thr	Val	Ile	His	Thr	Val	G1n	Ser	Ala	Pro	Gly	
		160					165					170				
cag	atg	ttc	tct	act	ссс	gcc	atc	cca	cct	atg	atg	tac	ccc	cac	ccc	638
Gln	Met	Phe	Ser	Thr	Pro	Ala	Ile	Pro	Pro	Met	Met	Tyr	Pro	His	Pro	
	175					180					185					
gcc	tat	ccg	atg	cct	ttc	atc	acc	acc	att	ctg	gga	ggg	ctg	tac	cca	686
Ala	Tyr	Pro	Met	Pro	Phe	Ile	Thr	Thr	Ile	Leu	Gly	Gly	Leu	Tyr	Pro	
190					195					200					205	
tcc	aag	tcc	atc	ctc	ctg	tca	ggc	act	gtc	ctg	ccc	agt	gct	cag	agg	734
Ser	Lys	Ser	Ile	Leu	Leu	Ser	Gly	Thr	Val	Leu	Pro	Ser	Ala	Gln	Arg	
				210					215					220		
ttc	cac	atc	aac	ctg	tgc	tct	ggg	aac	cac	atc	gcc	ttc	cac	ctg	aac	782
Phe	His	Ile	Asn	Leu	Cys	Ser	Gly	Asn	His	Ile	Ala	Phe	His	Leu	Asn	
			225					230					235			

ccc	cgt	ttt	gat	gag	aat	gct	gtg	gtc	cgc	aac	acc	cag	atc	gac	aac	830
Pro	Arg	Phe	Asp	Glu	Asn	Ala	Val	Val	Arg	Asn	Thr	Gln	Ile	Asp	Asn	
		240					245					250				
tcc	tgg	ggg	tct	gag	gag	cga	agt	ctg	ссс	cga	aaa	atg	ccc	ttc	gtc	878
Ser	Trp	Gly	Ser	Glu	Glu	Arg	Ser	Leu	Pro	Arg	Lys	Met	Pro	Phe	Val	
	255					260					265					
cgt	ggc	cag	agc	ttc	tca	gtg	tgg	atc	ttg	tgt	gaa	gct	cac	tgc	ctc	926
Arg	G1y	G1n	Ser	Phe	Ser	Val	Trp	Ile	Leu	Cys	Glu	Ala	His	Cys	Leu	
270					275					280					285	
aag	gtg	gcc	gtg	gat	ggt	cag	cac	ctg	ttt	gaa	tac	tac	cat	cgc	ctg	974
Lys	Val	Ala	Val	Asp	Gly	Gln	His	Leu	Phe	Glu	Tyr	Tyr	His	Arg	Leu	
				290					295					300		
agg	aac	ctg	ccc	acc	atc	aac	aga	ctg	gaa	gtg	ggg	ggc	gac	atc	cag	1022
Arg	Asn	Leu	Pro	Thr	Ile	Asn	Arg	Leu	Glu	Val	Gly	Gly	Asp	Ile	Gln	
			305					310					315			
ctg	acc	cat	gtg	cag	aca	tag	gcggo	ctt d	cctgg	gccct	tg g	ggccį	gggg	g		1070
Leu	Thr	His	Val	G1n	Thr											
		320														
ctg	gggtį	gtg į	gggca	agtci	tg gg	gtcc	tctca	a tca	atcc	ccac	ttc	ccag	gcc	cagc	ctttcc	1130
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ggci	taca	gcc a	accc	tgga	ac g	gagaa	aggca			ggg	att	gcct	tcc	tcago	ccgcag	1250
								520/	735							

cagcacctgg ggctccagct gctggaatcc taccatecca ggaggcaggc acagccaggg 1310
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gcagctccac cccagtccca agccaccagc tgtctgctcc tggtgggagg tggcctcctc 1430
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ccctcctgga aagcaggcct gatggcttcc cactggcctc caccacctga ccagagtgtt 1550
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<210> 143

<211> 136

<212> PRT

<213> Homo sapiens

**∠400> 143** 

Met Ala Gly Ala Ile Ile Glu Asn Met Ser Thr Lys Lys Leu Cys Ile

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Val Gly Gly Ile Leu Leu Val Phe Gln Ile Ile Ala Phe Leu Val Gly
20 25 30

Gly Leu Ile Ala Pro Gly Pro Thr Thr Ala Val Ser Tyr Met Ser Val 521/735

35 40 45

Lys Cys Val Asp Ala Arg Lys Asn His His Lys Thr Lys Trp Phe Val
50 55 60

Pro Trp Gly Pro Asn His Cys Asp Lys Ile Arg Asp Ile Glu Glu Ala
65 70 75 80

Ile Pro Arg Glu Ile Glu Ala Asn Asp Ile Val Phe Ser Val His Ile

85 90 95

Pro Leu Pro His Met Ala Leu Ser Cys Gly Phe Leu Asp Gln Arg His
100 105 110

Gly His Leu Ser Val Cys Leu Leu Thr Val Ala Phe Gly Gly Arg Phe 115 120 125

Leu Gln Pro Leu Met His Cys Val

<210> 144

<211> 1252

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (225).. (632)

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ccca	ıgaaa	ngg a	aggcg	gagga	na gg	gaggg	gagtg	tg1	tgaga	ngga	ggga	agcaa	aaa a	agcto	accet	180
aaaa	catt	ta 1	tttca	agga	ng aa	aaaga	aaaa	ggg	gggg	gcgc	aaaa	a ata	g gc	t ggg	g gca	236
												Met	t Ala	a Gly	7 Ala	
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														•		
att	ata	gaa	aac	atg	agc	acc	aag	aag	ctg	tgc	att	gtt	ggt	ggg	att	284
Ile	Ile	Glu	Asn	Met	Ser	Thr	Lys	Lys	Leu	Cys	Ile	Val	Gly	Gly	Ile	
5					10					15					20	
ctg	ctc	gtg	ttc	caa	atc	atc	gcc	ttt	ctg	gtg	gga	ggc	ttg	att	gct	332
Leu	Leu	Val	Phe	Gln	Ile	Ile	Ala	Phe	Leu	Val	Gly	Gly	Leu	Ile	Ala	
				25					30					35		
cca	ggg	ccc	aca	acg	gca	gtg	tcc	tac	atg	tcg	gtg	aaa	tgt	gtg	gat	380
Pro	Gly	Pro	Thr	Thr	Ala	Val	Ser	Tyr	Met	Ser	Val	Lys	Cys	Val	Asp	
			40					45					50			
gcc	cgt	aag	aac	cat	cac	aag	aca	aaa	tgg	ttc	gtg	cct	tgg	gga	ccc	428
Ala	Arg	Lys	Asn	His	His	Lys	Thr	Lys	Trp	Phe	Val	Pro	Trp	Gly	Pro	
		55					60					65				

aat cat tgt gac aag atc cga gac att gaa gag gca att cca agg gaa 476 523/735

Asn His Cys Asp Lys Ile Arg Asp Ile Glu Glu Ala Ile Pro Arg Glu
70 75 80

att gaa gcc aat gac atc gtg ttt tct gtt cac att ccc ctc ccc cac 524

Ile Glu Ala Asn Asp Ile Val Phe Ser Val His Ile Pro Leu Pro His

85 90 95 100

atg gct ctt agc tgt ggt ttc ttg gac cag cgg cat gga cat ttg tca 572

Met Ala Leu Ser Cys Gly Phe Leu Asp Gln Arg His Gly His Leu Ser

105 110 115

gtt tgc ctt ctg acg gta gct ttt gga gga aga ttc ctg cag cca cta 620 Val Cys Leu Leu Thr Val Ala Phe Gly Gly Arg Phe Leu Gln Pro Leu 120 125 130

atg cat tgt gta tgataacaaa aactctggta tgacacattt tctgtgatca 672 Met His Cys Val

135

ttgttaatta gtgacatagt aacatctgta gcagctggtt agtaaacctc atgtggggt 732
ggggtggggg tgtattcctt gggggatggt ttgggccgaa tggggagtgg aatatttgac 792
attttcctg ttttaaattc taggatagat tttaacatcc tttgcggtcc cagtccaagg 852
taggctggtg tcatagtctt ctcactccta atccatgacc actgttttt tcctatttat 912
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<210> 145

<211> 468

<212> PRT

<213> Homo sapiens

<400> 145

Met Pro Val Arg Thr Ile Thr Arg Gln Asn Gly Ser Cys Leu Gly Asp

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Pro Ile Ile Val Thr Arg Ser Glu Thr Leu Lys Arg Gln Phe Gln Phe
20 25 30

Met Leu Phe Ile Leu Gln Leu Asp Ile Ala Phe Lys Leu Asn Asn Gln
35 40 45

Ile Arg Glu Asn Ala Glu Val Ser Met Asp Val Ser Leu Ala Tyr Arg
50 55 60

WO 02/053737	PCT/JP01/11389

Asp	Asp	Ala	Phe	Ala	Glu	Trp	Thr	Glu	Met	Ala	His	Glu	Arg	Val	Pro
65					70					75					80

Arg Lys Leu Lys Cys Thr Phe Thr Ser Pro Lys Thr Pro Glu His Glu 85 90 95

Gly Arg Tyr Tyr Glu Cys Asp Val Leu Pro Phe Met Glu Ile Gly Ser 100 105 110

Val Ala His Lys Phe Tyr Leu Leu Asn Ile Arg Leu Pro Val Asn Glu 115 120 125

Lys Lys Ile Asn Val Gly Ile Gly Glu Ile Lys Asp Ile Arg Leu
130 135 140

Val Gly Ile His Gln Asn Gly Gly Phe Thr Lys Val Trp Phe Ala Met 145 150 155 160

Lys Thr Phe Leu Thr Pro Ser Ile Phe Ile Ile Met Val Trp Tyr Trp

165 170 175

Arg Arg Ile Thr Met Met Ser Arg Pro Pro Val Leu Leu Glu Lys Val 180 185 190

Ile Phe Ala Leu Gly Ile Ser Met Thr Phe Ile Asn Ile Pro Val Glu 195 200 205

Trp Phe Ser Ile Gly Phe Asp Trp Thr Trp Met Leu Leu Phe Gly Asp
210 215 220
526/735

Ile	Arg	Gln	Gly	Ile	Phe	Tyr	Ala	Met	Leu	Leu	Ser	Phe	Trp	Ile	Ile
225					230					235					240
Phe	Cys	G1y	Glu	His	Met	Met	Asp	G1n	His	Glu	Arg	Asn	His	Ile	Ala
				245					250					255	
Gly	Tyr	Trp	Lys	Gln	Val	Gly	Pro	Ile	Ala	Val	Gly	Ser	Phe	Cys	Leu
-	-	-	260			-		265					270	·	
Phe	Tle	Phe	Asp	Met.	Cvs	Glu	Arø	G1v	Va1	G1 n	Leu	Thr	Asn	Pro	Phe
1110	110	275	пор		0,0	014	280	01)		<b>01</b> 11	Dou	285		110	1 1.0
		2.0					200					200			
Т	S	T1.	Т	Tha	<b>Th.</b>	Aan	Tla	C1**	The	C1	ĭ	410	Ma+	410	Dho
1 ) 1		116	irp	1111	1111		116	GIY	1111	GIU		Ala	Met	nia	rne
	290					295					300				
						_		_		<b></b>	<b>5</b> 1		ro.1	_	
	lle	Val	Ala	Gly		Cys	Leu	Cys	Leu		Phe	Leu	Phe	Leu	
305					310					315					320
Phe	Met	Val	Phe	Gln	Val	Phe	Arg	Asn	Ile	Ser	Gly	Lys	Gln	Ser	Ser
				325					330					335	
Leu	Pro	Ala	Met	Ser	Lys	Val	Arg	Arg	Leu	His	Tyr	Glu	Gly	Leu	Ile
			340					345					350		
Phe	Arg	Phe	Lys	Phe	Leu	Met	Leu	Ile	Thr	Leu	Ala	Cys	A1a	Ala	Met

Thr Val Ile Phe Phe Ile Val Ser Gln Val Thr Glu Gly His Trp Lys \$527/735\$

360

365

355

370 375 380

Trp Gly Gly Val Thr Val Gln Val Asn Ser Ala Phe Phe Thr Gly Ile 385 390 395 400

Tyr Gly Met Trp Asn Leu Tyr Val Phe Ala Leu Met Phe Leu Tyr Ala
405 410 415

Pro Ser His Lys Asn Tyr Gly Glu Asp Gln Ser Asn Gly Met Gln Leu
420 425 430

Pro Cys Lys Ser Arg Glu Asp Cys Ala Leu Phe Val Ser Glu Leu Tyr
435
440
445

Gln Glu Leu Phe Ser Ala Ser Lys Tyr Ser Phe Ile Asn Asp Asn Ala 450 455 460

Ala Ser Gly Ile

465

<210> 146

<211> 1943

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (379).. (1782)

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ggcgccttcc gtcccggtcc catcctcgcc gcgctccagc acctctgaag ttttgcagcg 120

cccagaaagg aggcgaggaa ggagggagtg tgtgagagga gggagcaaaa agctcaccct 180

aaaacattta tttcaaggag aaaagaaaaa gggggggcgc aaaaatggct ggggcaatta 240

tagaaaacat gagcaccaag aagctgtgca ttgttggtgg gattctgctc gtgttccaaa 300

tcatcgcctt tctggtggga ggcttgattg ctccagggcc cacaacggca gtgtcctaca 360

tgtcggtgaa atgtgtgg atg ccc gta aga acc atc aca aga caa aat ggt 411

Met Pro Val Arg Thr Ile Thr Arg Gln Asn Gly

1 5 10

tcg tgc ctt ggg gac cca atc att gtg aca aga tcc gag aca ttg aag 459

tcg tgc ctt ggg gac cca atc att gtg aca aga tcc gag aca ttg aag 459
Ser Cys Leu Gly Asp Pro Ile Ile Val Thr Arg Ser Glu Thr Leu Lys

15 20 25

agg caa ttc caa ttc atg ctg ttt atc ctg cag ctg gac att gcc ttc 507

Arg Gln Phe Gln Phe Met Leu Phe Ile Leu Gln Leu Asp Ile Ala Phe
30 35 40

aag cta aac aac caa atc aga gaa aat gca gaa gtc tcc atg gac gtt 555 Lys Leu Asn Asn Gln Ile Arg Glu Asn Ala Glu Val Ser Met Asp Val

tcc	ctg	gct	tac	cgt	gat	gac	gcg	ttt	gct	gag	tgg	act	gaa	atg	gcc	603
Ser	Leu	Ala	Tyr	Arg	Asp	Asp	Ala	Phe	Ala	Glu	Trp	Thr	Glu	Met	Ala	
60					65					70					75	
cat	gaa	aga	gta	cca	cgg	aaa	ctc	aaa	tgc	acc	ttc	aca	tct	ccc	aag	651
His	G1u	Arg	Val	Pro	Arg	Lys	Leu	Lys	Cys	Thr	Phe	Thr	Ser	Pro	Lys	
				80					85					90		
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act	cca	gag	cat	gag	ggc	cgt	tac	tat	gaa	tgt	gat	gtc	ctt	cct	ttc	699
Thr	Pro	Glu	His	Glu	G1y	Arg	Tyr	Tyr	Glu	Cys	Asp	Val	Leu	Pro	Phe	
			95					100					105			
atg	gaa	att	ggg	tct	gtg	gcc	cat	aag	ttt	tac	ctt	tta	aac	atc	cgg	747
Met	Glu	Ile	Gly	Ser	Val	Ala	His	Lys	Phe	Tyr	Leu	Leu	Asn	Ile	Arg	
		110					115					120				
ctg	cct	gtg	aat	gag	aag	aag	aaa	atc	aat	gtg	gga	att	ggg	gag	ata	795
Leu	Pro	Val	Asn	Glu	Lys	Lys	Lys	Ile	Asn	Val	Gly	Ile	Gly	G1u	Ile	
	125					130					135					
														acc		843
Lys	Asp	Ile	Arg	Leu	Val	Gly	Ile	His	Gln	Asn	Gly	Gly	Phe	Thr	Lys	
140					145					150					155	
														atc		891
Val	Trp	Phe	Ala		Lys	Thr	Phe	Leu		Pro	Ser	Ile	Phe	Ile	Ile	
				160					165					170		

atg	gtg	tgg	tat	tgg	agg	agg	atc	acc	atg	atg	tcc	cga	ccc	cca	gtg	939
Met	Val	Trp	Tyr	Trp	Arg	Arg	Ile	Thr	Met	Met	Ser	Arg	Pro	Pro	Val	
			175					180					185		-	
ctt	ctg	gaa	aaa	gtc	atc	ttt	gcc	ctt	ggg	att	tcc	atg	acc	ttt	atc	987
Leu	Leu	Glu	Lys	Val	Ile	Phe	Ala	Leu	Gly	Ile	Ser	Met	Thr	Phe	Ile	
		190					195					200				
aat	atc	cca	gtg	gaa	tgg	ttt	tcc	atc	ggg	ttt	gac	tgg	acc	tgg	atg	1035
Asn	Ile	Pro	Val	Glu	Trp	Phe	Ser	Ile	Gly	Phe	Asp	Trp	Thr	Trp	Met	
	205					210					215					
ctg	ctg	ttt	ggt	gac	atc	cga	cag	ggc	atc	ttc	tat	gcg	atg	ctt	ctg	1083
Leu	Leu	Phe	G1y	Asp	Ile	Arg	Gln	Gly	Ile	Phe	Tyr	Ala	Met	Leu	Leu	
220					225					230					235	
							•									
tcc	ttc	tgg	atc	atc	ttc	tgt	ggc	gag	cac	atg	atg	gat	cag	cac	gag	1131
Ser	Phe	Trp	Ile	Ile	Phe	Cys	Gly	Glu	His	Met	Met	Asp	Gln	His	Glu	
				240					245					250		
cgg	aac	cac	atc	gca	ggg	tat	tgg	aag	caa	gtc	gga	ссс	att	gcc	gtt	1179
Arg	Asn	His	Ile	Ala	G1y	Tyr	Trp	Lys	G1n	Va1	Gly	Pro	Ile	Ala	Val	
			255					260					265	•		
ggc	tcc	ttc	tgc	ctc	ttc	ata	ttt	gac	atg	tgt	gag	aga	ggg	gta	caa	1227
Gly	Ser	Phe	Cys	Leu	Phe	Ile	Phe	Asp	Met	Cys	G1u	Arg	Gly	Val	Gln	
		270					275					280				
ctc	acg	aat	ccc	ttc	tac	agt	atc	tgg	act	aca	gac	att	gga	aca	gag	1275
								531/	735							

Leu Thr Asn Pro Phe Tyr Ser Ile Trp Thr Thr Asp Ile Gly Thr Glu ctg gcc atg gcc ttc atc atc gtg gct gga atc tgc ctc tgc ctc tac Leu Ala Met Ala Phe Ile Ile Val Ala Gly Ile Cys Leu Cys Leu Tyr ttc ctg ttt cta tgc ttc atg gta ttt cag gtg ttt cgg aac atc agt Phe Leu Phe Leu Cys Phe Met Val Phe Gln Val Phe Arg Asn Ile Ser ggg aag cag tcc agc ctg cca gct atg agc aaa gtc cgg cgg cta cac Gly Lys Gln Ser Ser Leu Pro Ala Met Ser Lys Val Arg Arg Leu His tat gag ggg cta att ttt agg ttc aag ttc ctc atg ctt atc acc ttg Tyr Glu Gly Leu Ile Phe Arg Phe Lys Phe Leu Met Leu Ile Thr Leu gcc tgc gct gcc atg act gtc atc ttc ttc atc gtt agt cag gta acg Ala Cys Ala Ala Met Thr Val Ile Phe Phe Ile Val Ser Gln Val Thr gaa ggc cat tgg aaa tgg ggc ggc gtc aca gtc caa gtg aac agt gcc Glu Gly His Trp Lys Trp Gly Gly Val Thr Val Gln Val Asn Ser Ala ttt ttc aca ggc atc tat ggg atg tgg aat ctg tat gtc ttt gct ctg Phe Phe Thr Gly Ile Tyr Gly Met Trp Asn Leu Tyr Val Phe Ala Leu 532/735

WO 02/053737			PCT/JP01/11389
	400	405	410

atg ttc ttg tat gca cca tcc cat aaa aac tat gga gaa gac cag tcc 1659

Met Phe Leu Tyr Ala Pro Ser His Lys Asn Tyr Gly Glu Asp Gln Ser

415 420 425

aat gga atg caa ctc cca tgt aaa tcg agg gaa gat tgt gct ttg ttt 1707 Asn Gly Met Gln Leu Pro Cys Lys Ser Arg Glu Asp Cys Ala Leu Phe 430 435 440

gtt tcg gaa ctt tat caa gaa ttg ttc agc gct tcg aaa tat tcc ttc 1755
Val Ser Glu Leu Tyr Gln Glu Leu Phe Ser Ala Ser Lys Tyr Ser Phe
445 450 455

atc aat gac aac gca gct tct ggt att tgagtcaaca aggcaacaca 1802 Ile Asn Asp Asn Ala Ala Ser Gly Ile 460 465

tgtttatcag ctttgcattt gcagttgtca cagtcacatt gattgtactt gtatacgcac 1862
acaaatacac tcatttagcc tttatctcaa aatgttaaat ataaggaaaa aagcgtcaac 1922
aataaatatt ctttgagtat t 1943

<210> 147

<211> 460

<212> PRT

<213> Homo sapiens

<400> 147

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1 5 10 15

Pro Ile Ile Val Thr Arg Ser Glu Thr Leu Lys Arg Gln Phe Gln Gly
20 25 30

Lys Leu Lys Pro Met Thr Ser Cys Phe Leu Phe Thr Phe Pro Ser Pro
35 40 45

Met Asp Val Ser Leu Ala Tyr Arg Asp Asp Ala Phe Ala Glu Trp Thr
50 55 , 60

Glu Met Ala His Glu Arg Val Pro Arg Lys Leu Lys Cys Thr Phe Thr
65 70 75 80

Ser Pro Lys Thr Pro Glu His Glu Gly Arg Tyr Tyr Glu Cys Asp Val 85 90 95

Leu Pro Phe Met Glu Ile Gly Ser Val Ala His Lys Phe Tyr Leu Leu 100 105 110

Asn Ile Arg Leu Pro Val Asn Glu Lys Lys Lys Ile Asn Val Gly Ile 115 120 125

Gly Glu IIe Lys Asp IIe Arg Leu Val Gly IIe His Gln Asn Gly Gly
130 135 140

Phe Thr Lys Val Trp Phe Ala Met Lys Thr Phe Leu Thr Pro Ser Ile 145 150 155 160

Phe Ile Ile Met Val Trp Tyr Trp Arg Arg Ile Thr Met Met Ser Arg 165 170 175

Pro Pro Val Leu Leu Glu Lys Val Ile Phe Ala Leu Gly Ile Ser Met 180 185 190

Thr Phe Ile Asn Ile Pro Val Glu Trp Phe Ser Ile Gly Phe Asp Trp

195 200 205

Thr Trp Met Leu Leu Phe Gly Asp Ile Arg Gln Gly Ile Phe Tyr Ala 210 215 220

Met Leu Leu Ser Phe Trp Ile Ile Phe Cys Gly Glu His Met Met Asp 225 230 235 240

Gln His Glu Arg Asn His Ile Ala Gly Tyr Trp Lys Gln Val Gly Pro 245 250 255

Ile Ala Val Gly Ser Phe Cys Leu Phe Ile Phe Asp Met Cys Glu Arg 260 265 270

Gly Val Gln Leu Thr Asn Pro Phe Tyr Ser Ile Trp Thr Thr Asp Ile 275 280 285

Gly Thr Glu Leu Ala Met Ala Phe Ile Ile Val Ala Gly Ile Cys Leu 290 295 300 535/735

Cys Leu Tyr Phe Leu Phe Leu Cys Phe Met Val Phe Gln Val Phe Arg Asn Ile Ser Gly Lys Gln Ser Ser Leu Pro Ala Met Ser Lys Val Arg Arg Leu His Tyr Glu Gly Leu Ile Phe Arg Phe Lys Phe Leu Met Leu Ile Thr Leu Ala Cys Ala Ala Met Thr Val Ile Phe Phe Ile Val Ser Gln Val Thr Glu Gly His Trp Lys Trp Gly Gly Ile Thr Val Gln Val Asn Ser Ala Phe Phe Thr Gly Ile Tyr Gly Met Trp Asn Leu Tyr Val Phe Ala Leu Met Phe Leu Tyr Ala Pro Ser His Lys Asn Tyr Gly Glu Asp Gln Ser Asn Gly Met Gln Leu Pro Cys Lys Ser Arg Glu Asp Cys Ala Leu Phe Val Ser Glu Leu Tyr Gln Glu Leu Phe Ser Ala Ser Lys 

Tyr Ser Phe Ile Asn Asp Asn Ala Ala Ser Gly Ile 536/735

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450 455 460

<210> 148

<211> 1919

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (376).. (1755)

<400> 148

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agaaaggagg egaggaagga gggagtgtat gagaaggagg agcaaaaage teaceetaaa 180
acatttattt eaaggagaaa agaaaaaggg ggggegeaaa aatggetggg geaattatag 240
aaaacatgag eaceaagaag etgtgeattg ttggtgggat tetgetegtg tteeaaatea 300
tegeetttet ggtgggagge ttgattgete eagggeeeac aaeggeagtg teetacatgt 360
eggtgaaatg tgtgg atg eee gta aga ace ate aca aga caa aat ggt teg 411
Met Pro Val Arg Thr Ile Thr Arg Gln Asn Gly Ser

537/735

5

10

1

tgc	ctt	ggg	gac	cca	atc	att	gtg	aca	aga	tcc	gag	aca	ttg	aag	agg	459
Cys	Leu	Gly	Asp	Pro	Ile	Ile	Val	Thr	Arg	Ser	Glu	Thr	Leu	Lys	Arg	
		15					20					25				. •
caa	ttc	caa	ggg	aaa	ttg	aag	cca	atg	aca	tcg	tgt	ttt	ctg	ttc	aca	507
Gln	Phe	Gln	Gly	Lys	Leu	Lys	Pro	Met	Thr	Ser	Cys	Phe	Leu	Phe	Thr	
	30					35					40					
ttc	ccc	tcc	ссс	atg	gac	gtt	tcc	ctg	gct	tac	cgt	gat	gac	gcg	ttt	555
Phe	Pṛo	Ser	Pro	Met	Asp	Val	Ser	Leu	Ala	Tyr	Arg	Asp	Asp	Ala	Phe	
45					50					55					60	
gct	gag	tgg	act	gaa	atg	gcc	cat	gaa	aga	gta	cca	cgg	aaa	ctc	aaa	603
Ala	Glu	Trp	Thr	Glu	Met	Ala	His	Glu	Arg	Val	Pro	Arg	Lys	Leu	Lys	
				65					70					75		
tgc	acc	ttc	aca	tct	ccc	aag	act	cca	gag	cat	gag	ggc	cgt	tac	tat	651
Cys	Thr	Phe	Thr	Ser	Pro	Lys	Thr	Pro	Glu	His	G1u	Gly	Arg	Tyr	Tyr	
			80					85					90			
gaa	tgt	gat	gtc	ctt	cct	ttc	atg	gaa	att	ggg	tct	gtg	gcc	cat	aag	699
Glu	Cys	Asp	Val	Leu	Pro	Phe	Met	Glu	Ile	Gly	Ser	Val	Ala	His	Lys	
		95					100					105				
ttt	tac	ctt	tta	aac	atc	cgg	ctg	cct	gtg	aat	gag	aag	aag	aaa	atc	747
Phe	Tyr	Leu	Leu	Asn	Ile	Arg	Leu	Pro	Val	Asn	Glu	Lys	Lys	Lys	Ile	
	110					115					120				•	
aat	gtg	gga	att	ggg	gag	ata	aag	gat		cgg	ttg	gtg	ggg	atc	cac	795
_								538/	/33							

Asn	Val	Gly	He	Gly	Glu	lie	Lys	Asp	TTe	Arg	Leu	Val	Gly	TIE	His	
125					130					135					140	
caa	aat	gga	ggc	ttc	acc	aag	gtg	tgg	ttt	gcc	atg	aag	acc	ttc	ctt	843
Gln	Asn	Gly	Gly	Phe	Thr	Lys	Val	Trp	Phe	Ala	Met	Lys	Thr	Phe	Leu	
				145					150					155		
acg	ccc	agc	atc	ttc	atc	att	atg	gtg	tgg	tat	tgg	agg	agg	atc	acc	891
Thr	Pro	Ser	Ile	Phe	Ile	Ile	Met	Val	Trp	Tyr	Trp	Arg	Arg	Ile	Thr	
			160					165					170			
atg	atg	tcc	cga	ссс	cca	gtg	ctt	ctg	gaa	aaa	gtc	atc	ttt	gcc	ctt	939
Met	Met	Ser	Arg	Pro	Pro	Val	Leu	Leu	Glu	Lys	Val	Ile	Phe	Ala	Leu	
		175					180					185				
ggg	att	tcc	atg	acc	ttt	atc	aat	atc	cca	gtg	gaa	tgg	ttt	tcc	atc	987
Gly	Ile	Ser	Met	Thr	Phe	Ile	Asn	Ile	Pro	Val	Glu	Trp	Phe	Ser	Ile	
	190					195					200					
ggg	ttt	gac	tgg	acc	tgg	atg	ctg	ctg	ttt	ggt	gac	atc	cga	cag	ggc	1035
Gly	Phe	Asp	Trp	Thr	Trp	Met	Leu	Leu	Phe	Gly	Asp	Ile	Arg	G1n	Gly	
205					210					215					220	
75																
	ttc	tat	gcg	atg	ctt	ctg	tcc	ttc	tgg	atc	atc	ttc	tgt	ggc	gag	1083
Île	Phe	Tyr	Ala	Met	Leu	Leu	Ser	Phe	Trp	Ile	Ile	Phe	Cys	Gly	G1u	
				225					230					235		
çac	atg	atg	gat	cag	cac	gag	cgg	aac	cac	atc	gca	ggg	tat	tgg	aag	1131
•			Asp													
			-					539/						-		

			240					245					250			
										•		44.	_4_	***		1170
					gcc											1179
G1n	Val	Gly	Pro	Ile	Ala	Val	Gly	Ser	Phe	Cys	Leu	Phe	Ile	Phe	Asp	
		255					260					265				
atg	tgt	gag	aga	ggg	gta	caa	ctc	acg	aat	ccc	ttc	tac	agt	atc	tgg	1227
Met	Cys	Glu	Arg	Gly	Va1	Gln	Leu	Thr	Asn	Pro	Phe	Tyr	Ser	Ile	Trp	
	270					275					280					
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act	aca	gac	att	gga	aca	gag	ctg	gcc	atg	gcc	ttc	atc	atc	gtg	gct	1275
Thr	Thr	Asp	Ile	Gly	Thr	Glu	Leu	Ala	Met	Ala	Phe	Ile	Ile	Val	Ala	
285					290					295					300	
gga	atc	tgc	ctc	tgc	ctc	tac	ttc	ctg	ttt	cta	tgc	ttc	atg	gta	ttt	1323
					Leu											
01)		0,0	202	305	2,4	-,-		200	310		-,-			315		
				300					010					010		
	_+_				-t-	+	~~~			+		o+ a	000	go+	0.1.5	1371
					atc						_	_	_			13/1
Gin	Val	Phe		Asn	Ile	Ser	GLy		GIN	Ser	Ser	Leu		АТА	met	
			320					325					330			
agc	aaa	gtc	cgg	cgg	cta	cac	tat	gag	ggg	cta	att	ttt	agg	ttc	aag	1419
Ser	Lys	Val	Arg	Arg	Leu	His	Tyr	Glu	Gly	Leu	Ile	Phe	Arg	Phe	Lys	
		335					340					345				
ttc	ctc	atg	ctt	atc	acc	ttg	gcc	tgc	gct	gcc	atg	act	gtc	atc	ttc	1467
Phe	Leu	Met	Leu	Ile	Thr	Leu	Ala	Cys	Ala	Ala	Met	Thr	Val	Ile	Phe	
	350					355					360					

540/735

PCT/JP01/11389

WO 02/053737

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Phe	Ile	Val	Ser	Gln	Val	Thr	Glu	Gly	His	Trp	Lys	Trp	Gly	Gly	Ile	
365					370					375					380	
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Thr	Val	G1n	Va1	Asn	Ser	Ala	Phe	Phe	Thr	Gly	Ile	Tyr	Gly	Met	Trp	
				385					390					395		
aat	ctg	tat	gtc	ttt	gct	ctg	atg	ttc	ttg	tat	gca	cca	tcc	cat	aaa	1611
Asn	Leu	Tyr	Val	Phe	Ala	Leu	Met	Phe	Leu	Tyr	Ala	Pro	Ser	His	Lys	
			400					405					410			
aac	tat	gga	gaa	gac	cag	tcc	aat	gga	atg	caa	ctc	cca	tgt	aaa	tcg	1659
Asn	Tyr	Gly	Glu	Asp	Gln	Ser	Asn	Gly	Met	Gln	Leu	Pro	Cys	Lys	Ser	
		415					420					425				
agg	gaa	gat	tgt	gct	ttg	ttt	gtt	tcg	gaa	ctt	tat	caa	gaa	ttg	ttc	1707
Arg	Glu	Asp	Cys	Ala	Leu	Phe	Val	Ser	Glu	Leu	Tyr	Gln	Glu	Leu	Phe	
	430					435					440					
agc	gct	tcg	aaa	tat	tcc	ttc	atc	aat	gac	aac	gca	gct	tct	ggt	att	1755
Ser	Ala	Ser	Lys	Tyr	Ser	Phe	Ile	Asn	Asp	Asn	Ala	Ala	Ser	Gly	Ile	
445					450					455					460	
tgag	gtcaa	aca a	aggca	aacao	a ta	gttta	atcag	g ctt	tgca	attt	gcag	gttgi	tca o	cagto	cacatt	1815
gati	tgtad	ett g	gtata	acgca	ac ac	caaat	tacad	tca	ittta	agcc	ttta	atcto	caa a	aatgi	ttaaat	1875

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1919

<210> 149

<211> 183

<212> PRT

<213> Homo sapiens

<400> 149

Met Lys Leu Leu Ser Leu Val Ala Val Gly Cys Leu Leu Val Pro

1 5 10 15

Pro Ala Glu Ala Asn Lys Ser Ser Glu Asp Ile Arg Cys Lys Cys Ile

20 25 30

Cys Pro Pro Tyr Arg Asn Ile Ser Gly His Ile Tyr Asn Gln Asn Val

35 40 45

Ser Gln Lys Asp Cys Asn Cys Leu His Val Val Glu Pro Met Pro Val

50 55 60

Pro Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys Glu Cys Arg Tyr

65 70 75 80

Glu Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile Val Ile Tyr Leu

85 90 95

Ser Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe Leu Met Leu Val

100 105 110

Asp Pro Leu Ile Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His Asn 115 120 125

Glu Glu Glu Asn Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Ser 130 135 140

Leu Gly Gly Pro Arg Ala Asn Thr Val Leu Glu Arg Val Glu Gly Ala
145 150 155 160

Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Thr Val Phe 165 170 175

Asp Arg His Lys Met Leu Ser 180

<210> 150

<211> 1562

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (120).. (668)

<400> 150

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WO 02/053737	PCT/JP01/11389

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aag	ctc	tta	tct	ttg	gtg	gct	gtg	gtc	ggg	tgt	ttg	ctg	gtg	ccc	167
Lys	Leu	Leu	Ser	Leu	Val	Ala	Val	Val	Gly	Cys	Leu	Leu	Val	Pro	
			5					10					15		
gct	gaa	gcc	aac	aag	agt	tct	gaa	gat	atc	cgg	tgc	aaa	tgc	atc	215
Ala	Glu	Ala	Asn	Lys	Ser	Ser	Glu	Asp	Ile	Arg	Cys	Lys	Cys	Ile	
		20					25					30			
cca	cct	tat	aga	aac	atc	agt	ggg	cac	att	tac	aac	cag	aat	gta	263
Pro	Pro	Tyr	Arg	Asn	Ile	Ser	Gly	His	Ile	Tyr	Asn	Gln	Asn	Val	
	35					40					45				
cag	aag	gac	tgc	aac	tgc	ctg	cac	gtg	gtg	gag	ccc	atg	cca	gtg	311
G1n	Lys	Asp	Cys	Asn	Cys	Leu	His	Val	Val	Glu	Pro	Met	Pro	Val	
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G1y	His	Asp	Val	Glu	Ala	Tyr	Cys	Leu	Leu	Cys	Glu	Cys	Arg	Tyr	
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gag	cgc	agc	acc	acc	acc	atc	aag	gtc	atc	att	gtc	atc	tac	ctg	407
Glu	Arg	Ser	Thr	Thr	Thr	Ile	Lys	Val	Ile	Ile	Val	Ile	Tyr	Leu	
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gtg	gtg	ggt	gcc	ctg	ttg	ctc	tac	atg	gcc	ttc	ctg	atg	ctg	gtg	455
Val	Val	Gly	Ala	Leu	Leu	Leu	Tyr	Met	Ala	Phe	Leu	Met	Leu	Val	
		100					105	/T2 5				110		•	
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Ala Asn Lys Ser         20       20         cca cct tat aga aac atc       Pro Pro Tyr Arg Asn Ile         35       35         cag aag gac tgc aac tgc       Gln Lys Asp Cys Asn Cys         50       55         ggc cat gac gtg gag gcc       Glu Ala         Gly His Asp Val Glu Ala       70         gag cgc agc acc acc acc       acc         Glu Arg Ser Thr Thr Thr       85         gtg gtg ggt gcc ctg ttg         Val Val Gly Ala Leu Leu	aag ctc tta tct ttg gtg gct Lys Leu Leu Ser Leu Val Ala 5  gct gaa gcc aac aag agt tct Ala Glu Ala Asn Lys Ser Ser 20  cca cct tat aga aac atc agt Pro Pro Tyr Arg Asn Ile Ser 35 40  cag aag gac tgc aac tgc ctg Gln Lys Asp Cys Asn Cys Leu 50 55  ggc cat gac gtg gag gcc tac Gly His Asp Val Glu Ala Tyr 70  gag cgc agc acc acc acc atc Glu Arg Ser Thr Thr Ile 85  gtg gtg ggt gcc ctg ttg ctc Val Val Gly Ala Leu Leu Leu	aag ctc       tta tct ttg gtg gct gtg         Lys Leu Leu Ser Leu Val Ala Val         gct gaa gcc aac aag agt tct gaa         Ala Glu Ala Asn Lys Ser Ser Glu         20       25         cca cct tat aga aac atc agt ggg         Pro Pro Tyr Arg Asn Ile Ser Gly         35       40         cag aag gac tgc aac tgc ctg cac         Gln Lys Asp Cys Asn Cys Leu His         50       55         ggc cat gac gtg gag gcc tac tgc         Gly His Asp Val Glu Ala Tyr Cys         70         gag cgc agc acc acc acc acc atc aag         Glu Arg Ser Thr Thr Thr Ile Lys         85         gtg gtg gtg gcc ctg ttg ctc tac         Val Val Gly Ala Leu Leu Leu Tyr         100	aag       ctc tta       tct ttg gtg gct gtg gtc         Lys       Leu Leu       Ser       Leu       Val       Ala       Val       Val         gct       gaa       gcc       aac       aag       agt       tct       gaa       gat         Ala       Glu       Ala       Asn       Lys       Ser       Ser       Glu       Asp         20       25       25       25       25       25       25       25       25       25       25       26       26       26       26       26       26       26       26     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tac tgc ctg ctg ctg Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys 70 75  gag cgc agc acc acc acc acc atc aag gtc atc att Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile 85 90  gtg gtg ggt ggt gcc ctg ttg ctc tac atg gcc ttc Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe 100 105	aag ctc tta tct ttg gtg gct gtg gtc ggg tgt ttg Lys Leu Leu Ser Leu Val Ala Val Val Gly Cys Leu 5 10  gct gaa gcc aac aag agt tct gaa gat atc cgg tgc Ala Glu Ala Asn Lys Ser Ser Glu Asp Ile Arg Cys 20 25  cca cct tat aga aac atc agt ggg cac att tac aac Pro Pro Tyr Arg Asn Ile Ser Gly His Ile Tyr Asn 35 40 45  cag aag gac tgc aac tgc ctg cac gtg gtg gag ccc Gln Lys Asp Cys Asn Cys Leu His Val Val Glu Pro 50 55 60  ggc cat gac gtg gag gcc tac tgc ctg tgc gag Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys Glu 70 75  gag cgc agc acc acc acc atc aag gtc atc att gtc Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile Val 85 90  gtg gtg ggt ggt gcc ctg Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe Leu 100 105	aag ctc tta tct ttg gtg gct gtg gtc ggg tgt ttg ctg Lys Leu Leu Ser Leu Val Ala Val Val Gly Cys Leu Leu 5	aag ctc tta tct ttg gtg gct gtg gtc ggg tgt ttg ctg gtg Lys Leu Leu Ser Leu Val Ala Val Val Gly Cys Leu Leu Val 5	gct gaa gcc aac aag agt tct gaa gat atc cgg tgc aaa tgc atc Ala Glu Ala Asn Lys Ser Ser Glu Asp Ile Arg Cys Lys Cys Ile 20

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Asp Pro Leu Ile Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His Asn
115 120 125

gag gag gag aat gag gat gct cgc tct atg gca gca gct gct gca tcc 551
Glu Glu Glu Asn Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Ser
130 135 140

ctc ggg gga ccc cga gca aac aca gtc ctg gag cgt gtg gaa ggt gcc 599
Leu Gly Gly Pro Arg Ala Asn Thr Val Leu Glu Arg Val Glu Gly Ala
145 150 155 160

cag cag cgg tgg aag ctg cag gtg cag gag cag cgg aag aca gtc ttc 647

Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Thr Val Phe

165 170 175

gat cgg cac aag atg ctc agc tagatgggct ggtgtggttg ggtcaaggcc 698
Asp Arg His Lys Met Leu Ser

180

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aggetgtegg tteggaacat gteteeacee acceeaceet etgtggetee aggetteatt 180
cteeceeate e atg gat aac eea ggg eet teg ete egt get gee ttt gge 230
Met Asp Asn Pro Gly Pro Ser Leu Arg Gly Ala Phe Gly

att cta ggt gcc ttg gaa agg gac agg ctg acc cac ctg aaa cac aag 278

Ile Leu Gly Ala Leu Glu Arg Asp Arg Leu Thr His Leu Lys His Lys

15 20 25

10

5

ctg ggg agt ctg tgt tca ggc agc cag gag tca aag ctt ctc cat gcc 326 Leu Gly Ser Leu Cys Ser Gly Ser Gln Glu Ser Lys Leu Leu His Ala 30 35 40 45

atg gta ctc ctg gct ctg ggc cag gac acg gag gcc agg gtc tct ctg 374

Met Val Leu Leu Ala Leu Gly Gln Asp Thr Glu Ala Arg Val Ser Leu

50 55 60

gag tcc ttg aag atg aac aca gta gcc cag ctg gta gcc cac cag tgg 422
Glu Ser Leu Lys Met Asn Thr Val Ala Gln Leu Val Ala His Gln Trp
65 70 75

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Ala	Asp	Met	Glu	Thr	Thr	Glu	Gly	Pro	Glu	Glu	Pro	Pro	Asp	Leu	Ser	
		80					85					90				
tgg	acg	gtg	gct	cgc	ctg	tac	cac	ctg	ctg	gct	gag	gag	aac	ctg	tgt	518
Trp	Thr	Val	Ala	Arg	Leu	Tyr	His	Leu	Leu	Ala	Glu	Glu	Asn	Leu	Cys	
	95					100					105					
ccg	gcc	tct	aca	agg	gac	atg	gct	tac	cag	gtg	gcc	ctt	cgt	gac	ttt	566
Pro	Ala	Ser	Thr	Arg	Asp	Met	Ala	Tyr	G1n	Val	Ala	Leu	Arg	Asp	Phe	
110					115					120					125	
gcc	tcc	cag	ggt	gac	cac	cag	ctg	ggc	caa	ctc	cag	aat	gag	gcc	tgg	614
Ala	Ser	Gln	Gly	Asp	His	Gln	Leu	Gly	Gln	Leu	Gln	Asn	Glu	Ala	Trp	
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gat	cgg	tgc	agt	tca	gat	atc	aag	ggg	gac	ccc	agt	ggt	ttc	cag	cca	662
Asp	Arg	Cys	Ser	Ser	Asp	Ile	Lys	Gly	Asp	Pro	Ser	Gly	Phe	Gln	Pro	
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	cat															710
Leu	His		His	Gln	Gly	Ser		Gln	Pro	Pro	Ser		Ser	Pro	Ala	
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	acc															758
Val	Thr	Arg	Ser	Gln	Pro	Arg	Pro	Ile	Asp	Thr	Pro	Asp	Trp	Ser	Trp	
	175					180					185					

190	gag				Ser 195	Thr	Asn	Ser	Thr		Ser	Leu	Ala	Ser	His	
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cta		atc	agc							200		•			205	
cta		atc	agc												-	
	Glu		-6-	cag	tca	ссс	act	ctt	gcc	ttt	ctc	tct	tca	cac	cat	854
Leu		Ile	Ser	G1n	Ser	Pro	Thr	Leu	Ala	Phe	Leu	Ser	Ser	His	His	
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gga	acc	cat	ggg	ccc	agc	aag	cta	tgt	aac	aca	ccg	ctg	gac	act	cag	902
Gly	Thr	His	Gly	Pro	Ser	Lys	Leu	Cys	Asn	Thr	Pro	Leu	Asp	Thr	Gln	
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gag	cct	cag	ctt	gtc	cct	gaa	ggc	tgc	caa	gaa	cct	gag	gag	ata	agc	950
Glu	Pro	Gln	Leu	Val	Pro	Glu	Gly	Cys	Gln	G1u	Pro	Glu	Glu	Ile	Ser	
		240					245					250				
tgg	cct	cca	tca	gtg	gag	acc	agt	gtc	tcc	tta	ggg	tta	cca	cac	gáa	998
Trp	Pro	Pro	Ser	Val	Glu	Thr	Ser	Val	Ser	Leu	Gly	Leu	Pro	His	Glu	
	255					260					265					
											tcg					1046
Ile	Ser	Val	Pro	Glu	Val	Ser	Pro	Glu	Glu		Ser	Pro	Ile	Leu		
270					275					280					285	
											tgt					1094
Asp	Ala	Leu	Ala		Pro	Asp	Thr	Ser		His	Cys	Pro	Ile		Cys	
				290					295					300		
			, .									<b>4</b> .				1140
aca	gag	ttg	tct	aca	aac	tcc	agg		/735	ctg	acg	tcc	acc	aca	gaa	1142

Thr	Glu	Leu	Ser 305	Thr	Asn	Ser	Arg	Ser 310	Pro	Leu	Thr	Ser	Thr 315	Thr	Glu	
agt	gtt	gga	aag	cag	tgg	cct	att	aca	agt	cag	agg	tca	cct	cag	gtt	1190
Ser	Val	Gly	Lys	Gln	Trp	Pro	Ile	Thr	Ser	Gln	Arg	Ser	Pro	G1n	Val	
		320					325					330				
cct	gta	gga	gat	gat	tct	ctg	cag	aac	acc	acg	tca	tcc	agc	cct	cct	1238
Pro	Val	Gly	Asp	Asp	Ser	Leu	Gln	Asn	Thr	Thr	Ser	Ser	Ser	Pro	Pro	
	335					340					345					
gcc	cag	cca	cca	tcc	ctc	caa	gcc	tcc	cct	aag	ctg	cct	cct	tcc	cct	1286
Ala	G1n	Pro	Pro	Ser	Leu	G1n	Ala	Ser	Pro	Lys	Leu	Pro	Pro	Ser	Pro	
350					355					360					365	
													cca			1334
Leu	Ser	Ser	Ala		Ser	Pro	Ser	Ser		Pro	Ala	Pro	Pro		Ser	
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													aaa Lys			1002
1111	Ser	110	385	Leu	лор	1112	261	390	1111	Dei	пор	UZII	395	1110	1,72	
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aac	ttt	gtg	gtt	atc	cat	gcc	agg	gct	gat	gaa	cag	gtg	gcc	cta	cgt	1430
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		400					405		_			410				
att	cgg	gag	aag	ctg	gag	acc	ctc	ggg	gta	cct	gac	ggg	gcc	acc	ttc	1478
Ile	Arg	G1u	Lys	Leu	Glu	Thr	Leu	Gly	Val	Pro	Asp	Gly	Ala	Thr	Phe	
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gtg gca aac acc ttc aag aca cag aag ctc cag gca cag cgg gta cgc 1814

Val Ala Asn Thr Phe Lys Thr Gln Lys Leu Gln Ala Gln Arg Val Arg

530 535 540

551/735

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Trp	Lys	Lys	Ala	Gln	Glu	Ala	Arg	Thr	Leu	Lys	Glu	Gln	Ser	Ile	Gln	
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ctg	gag	gca	gag	cgg	caa	aac	gtg	gca	gcc	ata	tct	gct	gcc	tac	aca	1910
Leu	G1u	Ala	G1u	Arg	Gln	Asn	Val	Ala	Ala	Ile	Ser	Ala	Ala	Tyr	Thr	
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gcc	tat	gtc	cat	agc	tat	agg	gcc	tgg	caa	gca	gag	atg	aac	aaa	ctt	1958
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Trp	Pro	G1y	Cys	Pro	G1n	Pro	Ile	Pro	Ser	His	Pro	Gln	Gly	Gly	Thr	
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cca	gtt	ttc	ССС	tat	tcc	cca	cag	cct	cca	tcc	ttc	cct	cag	cct	cca	2102
Pro	Val	Phe	Pro	Tyr	Ser	Pro	Gln	Pro	Pro	Ser	Phe	Pro	Gln	Pro	Pro	
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Cys	Phe	Pro	G1n	Pro	Pro	Ser	Phe	Pro	G1n	Pro	Pro	Ser	Phe	Pro	Leu	
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Pro	Pro	Val	Ser	Ser	Pro	Gln	Ser	Gln	Ser	Phe	Pro	Ser	Ala	Ser	Ser	
	655					660					665					
cca	gcc	cca	cag	act	cca	gga	cct	cag	cct	ctc	att	att	cac	cat	gcc	2246
Pro	Ala	Pro	Gln	Thr	Pro	Gly	Pro	Gln	Pro	Leu	Ile	Ile	His	His	Ala	
670					675					680					685	
cag	atg	gtt	cag	ctg	ggt	gtc	aac	aat	cac	atg	tgg	ggc	cac	aca	ggg	2294
G1n	Met	Va1	Gln	Leu	Gly	Val	Asn	Asn	His	Met	Trp	Gly	His	Thr	Gly	
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gcc	cag	tca	tct	gat	gac	aag	act	gag	tgt	tcg	gag	aac	ccc	tgt	atg	2342
Ala	G1n	Ser	Ser	Asp	Asp	Lys	Thr	Glu	Cys	Ser	Glu	Asn	Pro	Cys	Met	
			705					710					715			
ggc	cct	ctg	act	gat	cag	ggc	gaa	ccc	ctt	ctt	gag	act	cca	gag		2387
Gly	Pro	Leu	Thr	Asp	Gln	Gly	Glu	Pro	Leu	Leu	Glu	Thr	Pro	Glu		
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gctt	gggg	etc o	ccaca	agtgs	go ta	attag	gttgg	g acc	ccago	cttg	agao	ccca	aga	ggcag	gggaag	2567
0	- 600							-	Ū	Ū	J					
acca	caco	eta 1	taaat	tcage	go ci	tggga	aaca	ı tgo	cagaa	aacc	ccat	tttga	aac	agac1	tgtggg	2627
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acto	caat	ct (	gaato	ectet	ta ta	ztggs	acaga	ı gg:	atgai	tggg	gcca	agagı	gca	cctci	tgaggt	2687
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ctggggagga tgcggtcccg gggcacatag ggagggtcct gttttataa taaagttatt 2807

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Lys Met Asn Thr Val Ala Gln Leu Val Ala His Gln Trp Ala Asp Met
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WO 02/053737	PCT/JP01/11389

G1u	Thr	Thr	Glu	Gly 85	Pro	G1u	G1u	Pro	Pro 90	Asp	Leu	Ser	Trp	Thr 95	Val
Ala	Arg	Leu	Tyr 100	His	Leu	Leu	Ala	Glu 105	Glu	Asn	Leu	Cys	Pro 110	Ala	Ser
Thr	Arg	Asp 115	Met	Ala	Tyr	G1n	Val 120	Ala	Leu	Arg	Asp	Phe 125	Ala	Ser	Gln
Gly	Asp 130	His	G1n	Leu	Gly	Gln 135	Leu	Gln	Asn	Glu	Ala 140	Trp	Asp	Arg	Cys
Ser 145	Ser	Asp	Ile	Lys	Gly 150	Asp	Pro	Ser	G1y	Phe 155	Gln	Pro	Leu	His	Ser 160
His	Gln	Gly	Ser	Leu 165	G1n	Pro	Pro	Ser	Ala 170	Ser	Pro	Ala	Val	Thr 175	Arg
Ser	G1n	Pro	Arg 180	Pro	Ile	Asp	Thr	Pro 185	Asp	Trp	Ser	Trp	Gly 190	His	Thr
Leu	His	Ser 195	Thr	Asn	Ser	Thr	Ala 200	Ser	Leu	Ala	Ser	His 205	Leu	Glu	Ile

Gly Pro Ser Lys Leu Cys Asn Thr Pro Leu Asp Thr Gln Glu Pro Gln 225 230 230 235 240 555/735

Ser Gln Ser Pro Thr Leu Ala Phe Leu Ser Ser His His Gly Thr His

220

215

210

Leu	Val	Pro	Glu	G1y 245	Cys	Gln	Glu	Pro	Glu 250	Glu	Ile	Ser	Trp	Pro 255	Pro
Ser	Val	Glu	Thr 260	Ser	Val	Ser	Leu	G1y 265	Leu	Pro	His	Glu	Ile 270	Ser	Val
Pro	Glu	Val 275	Ser	Pro	Glu	Glu	Ala 280	Ser	Pro	Ile	Leu	Pro 285	Asp	Ala	Leu
Ala	Ala 290	Pro	Asp	Thr	Ser	Val 295	His	Cys	Pro	Ile	Glu 300	Cys	Thr	Glu	Leu
Ser 305	Thr	Asn	Ser	Arg	Ser 310	Pro	Leu	Thr	Ser	Thr 315	Thr	Glu	Ser	Val	Gly 320
Lys	Gln	Trp	Pro	Ile 325	Thr	Ser	Gln	Arg	Ser 330	Pro	Gln	Val	Pro	Val 335	Gly
Asp	Asp	Ser	Leu 340	Gln	Asn	Thr	Thr	Ser 345	Ser	Ser	Pro	Pro	Ala 350	Gĺn	Pro
Pro	Ser	Leu 355	Gln	Ala	Ser	Pro	Lys 360	Leu	Pro	Pro	Ser	Pro 365	Leu	Ser	Ser
Ala	Ser 370	Ser	Pro	Ser	Ser	Tyr 375	Pro	Ala	Pro	Pro	Thr 380	Ser	Thr	Ser	Pro

Val Leu Asp His Ser Glu Thr Ser Asp Gln Lys Phe Tyr Asn Phe Val

W	O 02/	05373	7												PCT/JP01/11389
385					390				J	395					400
Val	Ile	His	Ala	Arg 405	Ala	Asp	G1u	Gln	Val 410	Ala	Leu	Arg	Ile	Arg 415	G1u
Lys	Leu	Glu	Thr 420	Leu	Gly	Val	Pro	Asp 425	Gly	Ala	Thr	Phe	Cys 430	Glu	Glu
Phe	Gln	Val 435	Pro	Gly	Arg	Gly	G1u 440	Leu	His	Cys	Leu	Gln 445	Asp	Ala	Ile
Asp	His 450	Ser	Gly	Phe	Thr	Ile 455	Leu	Leu	Leu	Thr	Ala 460	Ser	Phe	Asp	Cys
Ser 465	Leu	Ser	Leu	His	Gln 470	Ile	Asn	His	Ala	Leu 475	Met	Asn	Ser	Leu	Thr 480
Gln	Ser	Gly	Arg	G1n 485	Asp	Cys	Val	Ile	Pro 490	Leu	Leu	Pro	Leu	Glu 495	Cys
Ser	Gln	Ala	Gln 500	Leu	Ser	Pro	Asp	Thr 505	Thr	Arg	Leu	Leu	His 510	Ser	Ile
Val	Trp	Leu 515	Asp	Glu	His	Ser	Pro 520	Ile	Phe	Ala	Arg	Lys 525	Val	Ala	Asn
Thr	Phe 530	Lys	Thr	G1n	Lys	Leu 535	Gln	Ala	G1n	Arg	Val 540	Arg	Trp	Lys	Lys

Ala Gln Glu Ala Arg Thr Leu Lys Glu Gln Ser Ile Gln Leu Glu Ala 545 550 555 560

Glu Arg Gln Asn Val Ala Ala Ile Ser Ala Ala Tyr Thr Ala Tyr Val
565 570 575

His Ser Tyr Arg Ala Trp Gln Ala Glu Met Asn Lys Leu Gly Val Ala 580 585 590

Phe Gly Lys Asn Leu Ser Leu Gly Thr Pro Thr Pro Ser Trp Pro Gly
595 600 605

Cys Pro Gln Pro Ile Pro Ser His Pro Gln Gly Gly Thr Pro Val Phe 610 615 620

Pro Tyr Ser Pro Gln Pro Pro Ser Phe Pro Gln Pro Pro Cys Phe Pro 625 630 635 640

Gln Pro Pro Ser Phe Pro Gln Pro Pro Ser Phe Pro Leu Pro Pro Val 645 650 655

Ser Ser Pro Gln Ser Gln Ser Phe Pro Ser Ala Ser Ser Pro Ala Pro 660 665 670

Gln Thr Pro Gly Pro Gln Pro Leu Ile Ile His His Ala Gln Met Val 675 680 685

Gln Leu Gly Val Asn Asn His Met Trp Gly His Thr Gly Ala Gln Ser 690 695 700 558/735

Ser Asp Asp Lys Thr Glu Cys Ser Glu Asn Pro Cys Met Gly Pro Leu 705 710 715 720

Thr Asp Gln Gly Glu Pro Leu Leu Glu Thr Pro Glu
725 730

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<212> DNA

<213> Homo sapiens

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<221> CDS

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<400> 153

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agcttctgct gccggaggct gcacccacct gtgccc atg gcc tgc aca ggc cca 114

Met Ala Cys Thr Gly Pro

1 5

tca ctt cct agc gcc ttc gac att cta ggt gca gca ggc cag gac aag 162 Ser Leu Pro Ser Ala Phe Asp Ile Leu Gly Ala Ala Gly Gln Asp Lys

10 . 15 . 20

ctc	ttg	tat	ctg	aag	cac	aaa	ctg	aag	acc	cca	cgc	cca	ggc	tgc	cag	210
Leu	Leu	Tyr	Leu	Lys	His	Lys	Leu	Lys	Thr	Pro	Arg	Pro	Gly	Cys	Gln	
		25					30					35				
ggg	cag	gac	ctc	ctg	cat	gcc	atg	gtt	ctc	ctg	aag	ctg	ggc	cag	gaa	258
Gly	Gln	Asp	Leu	Leu	His	Ala	Met	Val	Leu	Leu	Lys	Leu	Gly	Gln	Glu	
	40					45					50					
act	gag	gcc	agg	atc	tct	cta	gag	gca	ttg	aag	gcc	gat	gcg	gtg	gcc	306
Thr	Glu	Ala	Arg	Ile	Ser	Leu	Glu	Ala	Leu	Lys	Ala	Asp	Ala	Val	Ala	
55					60					65					70	
cgg	ctg	gtg	gcc	cgc	cag	tgg	gct	ggc	gtg	gac	agc	acc	gag	gac	cca	354
Arg	Leu	Val	Ala	Arg	Gln	Trp	Ala	Gly	Val	Asp	Ser	Thr	Glu	Asp	Pro	
				75					80					85	,	
gag	gag	ccc	cca	gat	gtg	tcc	tgg	gct	gtg	gcc	cgc	ttg	tac	cac	ctg	402
Glu	Glu	Pro	Pro	Asp	Val	Ser	Trp	Ala	Val	Ala	Arg	Leu	Tyr	His	Leu	
			90				•	95					100			
ctg	gct	gag	gag	aag	ctg	tgc	ccc	gcc	tcg	ctg	cgg	gac	gtg	gcc	tac	450
Leu	Ala	Glu	G1u	Lys	Leu	Cys	Pro	Ala	Ser	Leu	Arg	Asp	Val	Ala	Tyr	
		105					110					115				
cag	gaa	gcc	gtc	cgc	acc	ctc	agc	tcc	agg	gac	gac	cac	cgg	ctg	ggg	498
Gln	Glu	Ala	Val	Arg	Thr	Leu	Ser	Ser	Arg	Asp	Asp	His	Arg	Leu	Gly	
	120					125					130					
															•	
gaa	ctt	cag	gat	gag	gcc	cga	aac	cgg 560/		ggg	tgg	gac	att	gct	ggg	546

Glu	Leu	Gln	Asp	Glu	Ala	Arg	Asn	Arg	Cys	Gly	Trp	Asp	Ile	Ala	Gly	
135					140					145					150	
gat	cca	ggg	agc	atc	cgg	acg	ctc	cag	tcc	aat	ctg	ggc	tgc	ctc	cca	594
Asp	Pro	Gly	Ser	Ile	Arg	Thr	Leu	G1n	Ser	Asn	Leu	Gly	Cys	Leu	Pro	
				155					160					165		
cca	tcc	tcg	gct	ttg	ccc	tct	ggg	acc	agg	agc	ctc	cca	cgc	ссс	att	642
Pro	Ser	Ser	Ala	Leu	Pro	Ser	G1y	Thr	Arg	Ser	Leu	Pro	Arg	Pro	Ile	
			170					175					180			
gac	ggt	gtt	tcg	gac	tgg	agc	caa	ggg	tgc	tcc	ctg	cga	tcc	act	ggc	690
Asp	Gly	Val	Ser	Asp	Trp	Ser	Gln	Gly	Cys	Ser	Leu	Arg	Ser	Thr	Gly	
		185					190					195				
agc	cct	gcc	tcc	ctg	gcc	agc	aac	ttg	gaa	atc	agc	cag	tcc	cct	acc	738
Ser	Pro	Ala	Ser	Leu	Ala	Ser	Asn	Leu	Glu	Ile	Ser	G1n	Ser	Pro	Thr	
	200					205					210					
atg	ccc	ttc	ctc	agc	ctg	cac	cgc	agc	cca	cat	ggg	ссс	agc	aag	ctc	786
Met	Pro	Phe	Leu	Ser	Leu	His	Arg	Ser	Pro	His	Gly	Pro	Ser	Lys	Leu	
215					220					225					230	
tgt	gac	gac	ссс	cag	gcc	agc	ttg	gtg	ссс	gag	cct	gtc	ccc	ggt	ggc	834
Cys	Asp	Asp	Pro	G1n	Ala	Ser	Leu	Val	Pro	G1u	Pro	Val	Pro	Gly	Gly	
				235					240					245		
tgc	cag	gag	cct	gag	gag	atg	agc	tgg	ccg	cca	tcg	ggg	gag	att	gcc	882
Cys	Gln	Glu	Pro	Glu	Glu	Met	Ser	Trp	Pro	Pro	Ser	Gly	Glu	Ile	Ala	
								561/	735							

age cea cea gag etg cea age cea cet cet ggg ett eec gaa gtg Ser Pro Pro Glu Leu Pro Ser Ser Pro Pro Pro Gly Leu Pro Glu Val gcc cca gat gca acc tcc act ggc ctc cct gat acc ccc gca gct cca Ala Pro Asp Ala Thr Ser Thr Gly Leu Pro Asp Thr Pro Ala Ala Pro gaa acc agc acc aac tac cca gtg gag tgc acc gag ggg tct gca ggc Glu Thr Ser Thr Asn Tyr Pro Val Glu Cys Thr Glu Gly Ser Ala Gly ccc cag tct ctc ccc ttg cct att ctg gag ccg gtc aaa aac ccc tgc Pro Gln Ser Leu Pro Leu Pro Ile Leu Glu Pro Val Lys Asn Pro Cys tct gtc aaa gac cag acg cca ctc caa ctt tct gta gaa gat acc acc Ser Val Lys Asp Gln Thr Pro Leu Gln Leu Ser Val Glu Asp Thr Thr tet eca aat ace aag eeg tge eea eet act eec ace ace eea gaa aca Ser Pro Asn Thr Lys Pro Cys Pro Pro Thr Pro Thr Thr Pro Glu Thr tee eet eet eet eet eet eet eet tea tet aet eet tgt tea get 

Ser Pro Pro Pro Pro Pro Pro Pro Ser Ser Thr Pro Cys Ser Ala

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cac	ctg	acc	ccc	tcc	tcc	ctg	ttc	cct	tcc	tcc	ctg	gaa	tca	tca	tcg	1266
His	Leu	Thr	Pro	Ser	Ser	Leu	Phe	Pro	Ser	Ser	Leu	Glu	Ser	Ser	Ser	
375					380					385					390	
gaa	cag	aaa	ttc	tat	aac	ttt	gtg	atc	ctc	cac	gcc	agg	gca	gac	gaa	1314
Glu	G1n	Lys	Phe	Tyr	Asn	Phe	Val	Ile	Leu	His	Ala	Arg	Ala	Asp	G1u	
				395					400					405		
cac	atc	gcc	ctg	cgg	gtt	cgg	gag	aag	ctg	gag	gcc	ctt	ggc	gtg	ccc	1362
His	Ile	Ala	Leu	Arg	Val	Arg	Glu	Lys	Leu	Glu	Ala	Leu	Gly	Val	Pro	
			410					415					420			
gac	ggg	gcc	acc	ttc	tgc	gag	gat	ttc	cag	gtg	ccg	ggg	cgc	ggg	gag ·	1410
Asp	Gly	Ala	Thr	Phe	Cys	G1u	Asp	Phe	Gln	Val	Pro	Gly	Arg	Gly	Glu	
		425					430					435				
ctg	agc	tgc	ctg	cag	gac	gcc	ata	gac	cac	tca	gct	ttc	atc	atc	cta	1458
Leu	Ser	Cys	Leu	G1n	Asp	Ala	Ile	Asp	His	Ser	Ala	Phe	Ile	Ile	Leu	
	440					445					450					
ctt	ctc	acc	tcc	aac	ttc	gac	tgt	cgc	ctg	agc	ctg	cac	cag	gtg	aac	1506
Leu	Leu	Thr	Ser	Asn	Phe	Asp	Cys	Arg	Leu	Ser	Leu	His	Gln	Val	Asn	
455					460					465					470	
														tgt		1554
Gln	Ala	Met	Met		Asn	Leu	Thr	Arg		Gly	Ser	Pro	Asp	Cys	Val	
				475					480					485		

atc	ccc	ttc	ctg	ccc	ctg	gag	agc	tcc	ccg	gcc	cag	ctc	agc	tcc	gac	1602
Ile	Pro	Phe	Leu	Pro	Leu	Glu	Ser	Ser	Pro	Ala	Gln	Leu	Ser	Ser	Asp	
			490					495					500			
acg	gcc	agc	ctg	ctc	tcc	ggg	ctg	gtg	cgg	ctg	gac	gaa	cac	tcc	cag	1650
Thr	Ala	Ser	Leu	Leu	Ser	Gly	Leu	Val	Arg	Leu	Asp	Glu	His	Ser	Gln	
		505					510					515				
atc	ttc	gcc	agg	aag	gtg	gcc	aac	acc	ttc	aag	ccc	cac	agg	ctt	cag	1698
Ile	Phe	Ala	Arg	Lys	Val	Ala	Asn	Thr	Phe	Lys	Pro	His	Arg	Leu	Gln	
	520					525					530					
gcc	cga	aag	gcc	atg	tgg	agg	aag	gaa	cag	gac	acc	cga	gcc	ctg	cgg	1746
Ala	Arg	Lys	Ala	Met	Trp	Arg	Lys	G1u	Gln	Asp	Thr	Arg	Ala	Leu	Arg	
535					540					<b>54</b> 5					550	
gaa	cag	agc	caa	cac	ctg	gac	ggt	gag	cgg	atg	cag	gcg	gcg	gca	ctg	1794
G1u	G1n	Ser	G1n	His	Leu	Asp	Gly	Glu	Arg	Met	G1n	Ala	Ala	Ala	Leu	
				555					560					565		
aac	gca	gcc	tac	tca	gcc	tac	ctc	cag	agc	tac	ttg	tcc	tac	cag	gça	1842
Asn	Ala	Ala	Tyr	Ser	Ala	Tyr	Leu	Gln	Ser	Tyr	Leu	Ser	Tyr	G1n	Ala	
			570					575					580			
cag	atg	gag	cag	ctc	cag	gtg	gct	ttt	ggg	agc	cac	atg	tca	ttt	ggg	1890
Gln	Met	Glu	G1n	Leu	Gln	Val	Ala	Phe	Gly	Ser	His	Met	Ser	Phe	Gly	
		585					590					595				
act	ggg	gcg	ccc	tat	ggg	gct	cga	atg	ccc	ttt	ggg	ggc	cag	gtg	ccc	1938
								564/	735							

Thr Gly Ala Pro Tyr Gly Ala Arg Met Pro Phe Gly Gly Gln Val Pro ctg gga gcc ccg cca ccc ttt ccc act tgg ccg ggg tgc ccg cag ccg Leu Gly Ala Pro Pro Pro Phe Pro Thr Trp Pro Gly Cys Pro Gln Pro cca ccc ctg cac gca tgg cag gct ggc acc ccc cca ccg ccc tcc cca Pro Pro Leu His Ala Trp Gln Ala Gly Thr Pro Pro Pro Pro Ser Pro cag cca gca gcc ttt cca cag tca ctg ccc ttc ccg cag tcc cca gcc Gln Pro Ala Ala Phe Pro Gln Ser Leu Pro Phe Pro Gln Ser Pro Ala ttc cct acg gcc tca ccc gca ccc cct cag agc cca ggg ctg caa ccc Phe Pro Thr Ala Ser Pro Ala Pro Pro Gln Ser Pro Gly Leu Gln Pro ctc att atc cac cac gca cag atg gta cag ctg ggg ctg aac aac cac Leu Ile Ile His His Ala Gln Met Val Gln Leu Gly Leu Asn Asn His atg tgg aac cag aga ggg tcc cag gcg ccc gag gac aag acg cag gag Met Trp Asn Gln Arg Gly Ser Gln Ala Pro Glu Asp Lys Thr Gln Glu gca gaa tgaccgcgtg tccttgcctg accacctggg gaacacccct ggacccaggc 

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Ala Glu

atcggccagg accccataga gcaccccggt ctgccctgtg ccctgtgac agtggaagat 2342 gaggtcatct gccacttca ggacattgtc cgggagccct tcatttagga caaaacgggc 2402 gcgatgatgc cctggcttc agggtggtca gaactggata cggtgttac aattccaatc 2462 tctctattc tgggtgaagg gtcttggtgg tgggggtatt gctacggtct tttaattata 2522 ataaatattt attgaatgct tc 2544

<210> 154

<211> 712

<212> PRT

<213> Homo sapiens

<400> 154

Met Ala Cys Thr Gly Pro Ser Leu Pro Ser Ala Phe Asp Ile Leu Gly

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Ala Ala Gly Gln Asp Lys Leu Leu Tyr Leu Lys His Lys Leu Lys Thr
20 25 30

Pro Arg Pro Gly Cys Gln Gly Gln Asp Leu Leu His Ala Met Val Leu
35 40 45

Leu Lys Leu Gly Gln Glu Thr Glu Ala Arg Ile Ser Leu Glu Ala Leu
50 55 60
566/735

Lys	Ala	Asp	Ala	Val	Ala	Arg	Leu	Val	Ala	Arg	GIn	Trp	Ala	Gly	Val
65					70					75					80
Asp	Ser	Thr	Glu	Asp	Pro	Glu	Glu	Pro	Pro	Asp	Val	Ser	Trp	Ala	Val
				85					90					95	
Ala	Arg	Leu	Tyr	His	Leu	Leu	Ala	Glu	Glu	Lys	Leu	Cys	Pro	Ala	Ser
•			100					105					110		
Leu	Arg		Val	Ala	Tyr	Gln		Ala	Val	Arg	Thr		Ser	Ser	Arg
		115					120					125			
Asp		His	Arg	Leu	G1y		Leu	G1n	Asp	G1u		Arg	Asn	Arg	Cys
	130					135					140				
	Trp	Asp	Ile	Ala		Asp	Pro	G1y	Ser	Ile	Arg	Thr	Leu	Gln	
145					150					155					160
Asn	Leu	Gly	Cys		Pro	Pro	Ser	Ser		Leu	Pro	Ser	Gly		Arg
				165					170					175	
Ser	Leu	Pro		Pro	Ile	Asp	Gly		Ser	Asp	Trp	Ser		Gly	Cys
			180					185					190		
Ser	Leu		Ser	Thr	Gly	Ser		Ala	Ser	Leu	Ala		Asn	Leu	Glu
		195					200					205			
Ile	Ser	Gln	Ser	Pro	Thr	Met	Pro	Phe 567/		Ser	Leu	His	Arg	Ser	Pro

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His Gly Pro Ser Lys Leu Cys Asp Asp Pro Gln Ala Ser Leu Val Pro Glu Pro Val Pro Gly Gly Cys Gln Glu Pro Glu Glu Met Ser Trp Pro Pro Ser Gly Glu Ile Ala Ser Pro Pro Glu Leu Pro Ser Ser Pro Pro Pro Gly Leu Pro Glu Val Ala Pro Asp Ala Thr Ser Thr Gly Leu Pro Asp Thr Pro Ala Ala Pro Glu Thr Ser Thr Asn Tyr Pro Val Glu Cys 

Thr Glu Gly Ser Ala Gly Pro Gln Ser Leu Pro Leu Pro Ile Leu Glu 305 310 315 320

Pro Val Lys Asn Pro Cys Ser Val Lys Asp Gln Thr Pro Leu Gln Leu . 325 330 335

Ser Val Glu Asp Thr Thr Ser Pro Asn Thr Lys Pro Cys Pro Pro Thr
340 345 350

Pro Thr Thr Pro Glu Thr Ser Pro Pro Pro Pro Pro Pro Pro Pro Ser

355 360 365

Ser Thr Pro Cys Ser Ala His Leu Thr Pro Ser Ser Leu Phe Pro Ser 370 375 380

Ser Leu Glu Ser Ser Ser Glu Gln Lys Phe Tyr Asn Phe Val Ile Leu 385 390 395 400

His Ala Arg Ala Asp Glu His Ile Ala Leu Arg Val Arg Glu Lys Leu
405 410 415

Glu Ala Leu Gly Val Pro Asp Gly Ala Thr Phe Cys Glu Asp Phe Gln
420 425 430

Val Pro Gly Arg Gly Glu Leu Ser Cys Leu Gln Asp Ala Ile Asp His
435
440
445

Ser Ala Phe Ile Ile Leu Leu Leu Thr Ser Asn Phe Asp Cys Arg Leu
450 455 460

Ser Leu His Gln Val Asn Gln Ala Met Met Ser Asn Leu Thr Arg Gln 465 470 475 480

Gly Ser Pro Asp Cys Val Ile Pro Phe Leu Pro Leu Glu Ser Ser Pro 485 490 495

Ala Gln Leu Ser Ser Asp Thr Ala Ser Leu Leu Ser Gly Leu Val Arg
500 505 510

Leu Asp Glu His Ser Gln Ile Phe Ala Arg Lys Val Ala Asn Thr Phe
515 520 525
569/735

Lys	Pro	His	Arg	Leu	G1n	Ala	Arg	Lys	Ala	Met	Trp	Arg	Lys	Glu	Gln
	530					535					540				•
Asp	Thr	Arg	Ala	Leu	Arg	Glu	Gln	Ser	Gln	His	Leu	Asp	Gly	Glu	Arg
545					550					555					560
Met	Gln	Ala	Ala	Ala	Leu	Asn	Ala	Ala	Tyr	Ser	Ala	Tyr	Leu	Gln	Ser
				565					570					575	
Tyr	Leu	Ser	Tyr	Gln	Ala	Gln	Met	Glu	G1n	Leu	Gln	Val	Ala	Phe	Gly
			580					585					590		
Ser	His		Ser	Phe	Gly	Thr		Ala	Pro	Tyr	G1y		Arg	Met	Pro
		595					600					605			
Phe		Gly	G1n	Val	Pro		Gly	Ala	Pro	Pro		Phe	Pro	Thr	Trp
_	610				_	615	_	_	•••		620	0.1	4.7	0.1	<b></b>
	Gly	Cys	Pro	G1n		Pro	Pro	Leu	His		Trp	GIn	Ala	Gly	
625					630					635	_				640
Pro	Pro	Pro	Pro	Ser	Pro	Gln	Pro	Ala		Phe	Pro	G1n	Ser		Pro
				645					650					655	
Phe	Pro	Gln		Pro	Ala	Phe	Pro		Ala	Ser	Pro	Ala		Pro	G1n
			660					665					670		

Ser Pro Gly Leu Gln Pro Leu Ile Ile His His Ala Gln Met Val Gln

675 680 685

Leu Gly Leu Asn Asn His Met Trp Asn Gln Arg Gly Ser Gln Ala Pro 690 695 700

Glu Asp Lys Thr Gln Glu Ala Glu 705 710

, <210> 155

<211> 3456

<212> DNA

<213> Homo sapiens

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<221> CDS

<222> (281).. (3016)

<400> 155

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ggaggagagc tctgtggatg gcaaagggga ccggaagagc acaggcctga aactctccaa 180

gaagaaagca aggaggagac acacggatga cccaagcaag gaatgcttca ctctgaaatt 240

tgacctgaat gtggacattg agacagagat cgtcccagcc atg aag aag tca 295 571/735

Met Lys Lys Lys Ser
1 5

ctg	ggg	gag	gtg	ctg	ctg	cct	gta	ttt	gaa	agg	aag	ggc	att	gcg	ctg	343
Leu	Gly	Glu	Val	Leu	Leu	Pro	Val	Phe	Glu	Arg	Lys	Gly	Ile	Ala	Leu	
				10					15					20		
ggc	aaa	gtg	gac	atc	tac	ctg	gac	cag	tcc	aac	aca	ссс	ctg	tcc	ctc	391
Gly	Lys	Val	Asp	Ile	Tyr	Leu	Asp	G1n	Ser	Asn	Thr	Pro	Leu	Ser	Leu	
			25					30					35			
acc	ttc	gag	gcc	tac	agg	ttc	ggg	gga	cac	tac	ctt	cgt	gtc	aaa	gcc	439
Thr	Phe	Glu	Ala	Tyr	Arg	Phe	Gly	Gly	His	Tyr	Leu	Arg	Val	Lys	Ala	
		40					45					50				
cca	gcc	aag	cct	gga	gat	gag	ggc	aag	gtg	gag	cag	ggc	atg	aag	gac	487
Pro	Ala	Lys	Pro	Gly	Asp	Glu	Gly	Lys	Val	Glu	Gln	Gly	Met	Lys	Asp	
	55					60					65					
tcc	aag	tcc	ctg	agt	ttg	ccg	att	ctg	cgg	cca	gct	ggg	acc	ggg	ccc	535
Ser	Lys	Ser	Leu	Ser	Leu	Pro	Ile	Leu	Arg	Pro	Ala	Gly	Thr	Gly	Pro	
70					75					80					85	
ccc	gcc	ctg	gag	cgt	gtg	gac	gcc	cag	agc	cgc	cgg	gag	agc	ctg	gac	583
Pro	Ala	Leu	Glu	Arg	Val	Asp	Ala	Gln	Ser	Arg	Arg	Glu	Ser	Leu	Asp	
				90					95					100		
atc	ttg	gcc	cct	ggc	cgc	cgc	cgc	aag	aac	atg	tcg	gag	ttc	ctg	ggg	631

Ile Leu Ala Pro Gly Arg Arg Lys Asn Met Ser Glu Phe Leu Gly

W	O 02/	05373	37												РСТ/Л	P01/1
			105					110					115			
gag	gcg	agc	atc	ccc	ggg	cag	gag	ccc	ccc	acg	ccc.	tcc	agc	tgc	tct	679
Glu	Ala	Ser	Ile	Pro	Gly	Gln	Glu	Pro	Pro	Thr	Pro	Ser	Ser	Cys	Ser	
		120					125					130				
ctg	ccc	agc	ggc	agc	agt	ggc	agc	acc	aac	act	ggc	gac	agc	tgg	aag	727
Leu	Pro	Ser	Gly	Ser	Ser	Gly	Ser	Thr	Asn	Thr	Gly	Asp	Ser	Trp	Lys	
	135					140					145					
aac	cgg	gcg	gcc	agt	cgc	ttc	agc	ggc	ttt	ttc	agc	tcc	ggc	ccc	agc	775
	Arg															
150					155					160					165	
acc	agc	gcc	ttt	ggc	cgg	gag	gta	gac	aag	atg	gag	cag	ctg	gag	ggc	823
Thr	Ser	Ala	Phe	Gly	Arg	Glu	Val	Asp	Lys	Met	Glu	Gln	Leu	Glu	Gly	
				170					175					180		
	ctg															871
Lys	Leu	His		Tyr	Ser	Leu	Phe		Leu	Pro	Arg	Leu	Pro	Arg	Gly	
			185					190					195			
ctg	cgc	ttc	gac	cat	gac	tcc	tgg	gag	gag	gag	tac	gat	gaa	gac	gag	919
Leu	Arg	Phe	Asp	His	Asp	Ser	Trp	G1u	Glu	Glu	Tyr	Asp	Glu	Asp	Glu	
		200					205					210				
gat	gag	gac	aat	gcc	tgc	ctg	agg	ctg	gag	gac	agc	tgg	cgg	gag	ctc	967
Asp	G111	Asp	Asn	Ala	Cvs	Len	Aro	Len	G111	Asn	Ser	Trp	Arø	G113	Leu	

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att	gat	ggg	cat	gag	aag	ctg	acc	cgg	cgg	cag	tgc	cac	cag	cag	gag	1015
Ile	Asp	Gly	His	Glu	Lys	Leu	Thr	Arg	Arg	G1n	Cys	His	Gln	Gln	Glu	
230					235					240					245	
gcg	gtg	tgg	gag	ctg	ctg	cac	acg	gag	gcc	tcc	tac	atc	agg	aaa	ctg	1063
Ala	Val	Trp	G1u	Leu	Leu	His	Thr	Glu	Ala	Ser	Tyr	Ile	Arg	Lys	Leu	
				250					255					260		
cgg	gtg	atc	atc	aac	ctg	ttc	ttg	tgc	tgc	ctc	ctg	aac	ctg	caa	gag	1111
Arg	Val	Ile	Ile	Asn	Leu	Phe	Leu	Cys	Cys	Leu	Leu	Asn	Leu	Gln	Glu	
			265					270					275			
tca	ggg	ctg	ctg	tgt	gag	gtg	gag	gcg	gag	cgc	ctg	ttc	agc	aac	atc	1159
Ser	Gly	Leu	Leu	Cys	Glu	Val	Glu	Ala	G1u	Arg	Leu	Phe	Ser	Asn	Ile	
		280					285					290				
ccg	gag	atc	gcg	cag	ctg	cac	cgc	agg	ctg	tgg	gct	agc	gtg	atg	gcg	1207
Pro	Glu	Ile	Ala	G1n	Leu	His	Arg	Arg	Leu	Trp	Ala	Ser	Val	Met	Ala	
	295					300					305					
ccg	gtg	ctg	gag	aag	gcg	cgg	cgc	acg	cga	gcg	ctg	cta	cag	ссс	ggg	1255
Pro	Val	Leu	Glu	Lys	Ala	Arg	Arg	Thr	Arg	Ala	Leu	Leu	G1n	Pro	Gly	
310					315					320					325	
gac	ttc	ctc	aaa	ggc	ttc	aag	atg	ttc	ggc	tcg	ctc	ttc	aag	ссс	tac	1303
Asp	Phe	Leu	Lys	Gly	Phe	Lys	Met	Phe	Gly	Ser	Leu	Phe	Lys	Pro	Tyr	
				330					335					340		

atc cgc tac tgc atg gag gag gag ggc tgc atg gag tac atg cgc ggc

Ile	Arg	Tyr	Cys	Met	Glu	Glu	Glu	Gly	Cys	Met	Glu	Tyr	Met	Arg	Gly	
			345					350					355			
ctg	ctg	cgc	gac	aac	gac	ctc	ttc	cgg	gcc	tac	atc	acg	tgg	gcg	gag	1399
Leu	Leu	Arg	Asp	Asn	Asp	Leu	Phe	Arg	Ala	Tyr	Ile	Thr	Trp	Ala	Glu	
		360					365					370				
aag	cac	cca	cag	tgc	cag	agg	ctg	aag	ctg	agc	gac	atg	ctg	gcc	aaa	1447
						Arg										
•	375			·		380					385					
ccc	cac	cag	CEE	ctc	acc	aag	tac	ccg	ctg	ctg	ctc	aag	tcg	gtg	ctg	1495
						Lys										
390		0211		200	395	2,0	-,-			400		_,-			405	
500										100					100	
200	994	200	asa.	aaa	CC 4	cgc	acc	9911	asa		atc	at c	acc	atσ	atc	1543
																1040
пВ	Lys	ш	Giu		LIO	Arg	nia	LyS		пта	Val	191	піа	420		
				410					415					420		
																1501
						atc										1591
Gly	Ser	Val		Arg	Phe	Ile	His		Val	Asn	Ala	Cys		Arg	Gln	
			425					430					435			
cgg	cag	gag	cgg	cag	cgg	ctg	gcg	gcc	gtg	gtg	agc	cgc	atc	gac	gcc	1639
Arg	G1n	Glu	Arg	G1n	Arg	Leu	Ala	Ala	Val	Val	Ser	Arg	Ile	Asp	Ala	
		440					445					450				
tac	gag	gtg	gtg	gaa	agc	agc	agc			gtg	gac	aag	ctc	ctg	aag	1687
								575/	735							

Tyr Glu Val Val Glu Ser Ser Ser Asp Glu Val Asp Lys Leu Leu Lys gaa ttt ctg cac ctg gac ttg aca gcg ccc atc cct ggc gcc tcc ccg Glu Phe Leu His Leu Asp Leu Thr Ala Pro Ile Pro Gly Ala Ser Pro gag gag acg cgg cag ctg ctg ctg gag ggg agc ctg agg atg aag gag Glu Glu Thr Arg Gln Leu Leu Leu Glu Gly Ser Leu Arg Met Lys Glu ggg aag gac agc aag atg gat gtg tac tgc ttc ctc ttc acg gat ctg Gly Lys Asp Ser Lys Met Asp Val Tyr Cys Phe Leu Phe Thr Asp Leu ctg ttg gtg acc aaa gca gtg aag aag gca gag agg acc agg gtc atc Leu Leu Val Thr Lys Ala Val Lys Lys Ala Glu Arg Thr Arg Val Ile agg cca ccc ctg ctc gtg gac aag att gtg tgc cgg gag cta cgg gac Arg Pro Pro Leu Leu Val Asp Lys Ile Val Cys Arg Glu Leu Arg Asp cct ggg tcc ttc ctc ctt atc tac ctg aat gag ttt cac agt gct gta Pro Gly Ser Phe Leu Leu Ile Tyr Leu Asn Glu Phe His Ser Ala Val ggg gcc tac acg ttc cag gcc agt ggc cag gcc ttg tgc cgt ggc tgg 

Gly Ala Tyr Thr Phe Gln Ala Ser Gly Gln Ala Leu Cys Arg Gly Trp

WO 02/053737 PCT/JP01/11389 gtg gac acc att tac aat gcc cag aac cag ctg caa cag ctg cgt gca Val Asp Thr Ile Tyr Asn Ala Gln Asn Gln Leu Gln Gln Leu Arg Ala cag gag ccc cca ggc agt cag cag ccc ctg cag agc ctg gaa gag gag Gln Glu Pro Pro Gly Ser Gln Gln Pro Leu Gln Ser Leu Glu Glu Glu ggc gag gac agt ggc act toa gct gcc agc toc cot acc atc atg cgg Gly Glu Asp Ser Gly Thr Ser Ala Ala Ser Ser Pro Thr Ile Met Arg aaa agc agc ggc agc ccc gac tct cag cac tgt gcc tca gat ggc tcc Lys Ser Ser Gly Ser Pro Asp Ser Gln His Cys Ala Ser Asp Gly Ser acg gag acc ctg gcc atg gtt gtg gta gag cct ggg gac acg ctg tcc Thr Glu Thr Leu Ala Met Val Val Val Glu Pro Gly Asp Thr Leu Ser 

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tcc ccc gag ttc gac agc ggt cct ttc agc tcc cag tct gat gag acc

Ser Pro Glu Phe Asp Ser Gly Pro Phe Ser Ser Gln Ser Asp Glu Thr

tct	ctc	agc	acc	act	gcc	tca	tct	gcc	acg	ccc	acc	agt	gag	ctg	ctg	2407
Ser	Leu	Ser	Thr	Thr	Ala	Ser	Ser	Ala	Thr	Pro	Thr	Şer	Glu	Leu	Leu	
	695					700					705					
ccc	ctg	ggt	ccg	gtg	gac	ggc	cgc	tcc	tgc	tcc	atg	gac	tct	gcc	tac	2455
Pro	Leu	G1y	Pro	Val	Asp	G1y	Arg	Ser	Cys	Ser	Met	Asp	Ser	Ala	Tyr	
710					715					720					725	
														•		
ggc	acc	ctc	tcc	cca	acc	tcc	tta	caa	gac	ttt	gtg	gcc	cca	ggc	cca	2503
Gly	Thr	Leu	Ser	Pro	Thr	Ser	Leu	Gln	Asp	Phe	Val	Ala	Pro	Gly	Pro	
				730					735					740		
	gca															2551
Met	Ala	Glu		Val	Pro	Arg	Ala		Glu	Ser	Pro	Arg		Pro	Ser	
			745					750					755			
																0.500
	cca															2599
Pro	Pro		Ser	Pro	Arg	Leu		Arg	Arg	Thr	Pro		Gin	Leu	Leu	
		760					765					770				
200	tgc	222	000	000	a+«	ata	224	+++	224	<b>+</b> 00	a a a	<b>700</b>	250	ata	oto	2647
	Cys															2041
961	775	110	110	1112	Leu	780	Lys	001	Lys	Der	785	nia	561	Leu	Leu	
	110					100					100					
cag	ctg	cte	gca	ggg	gct	ggc	acc	cat	ggg	aca	ccc	tct	gcc	ccc	agc	2695
	Leu															223
790			,	,	795				,	800	- <del>-</del>	<del>-</del>		. –	805	
- •															_	

cgc agc ctg tca gag ctc tgc ctg gct gtt cca gcc cca ggt att agg Arg Ser Leu Ser Glu Leu Cys Leu Ala Val Pro Ala Pro Gly Ile Arg act cag ggc tcc cct cag gaa gct ggg ccc agc tgg gat tgc cga ggg Thr Gln Gly Ser Pro Gln Glu Ala Gly Pro Ser Trp Asp Cys Arg Gly gee eet age eet gge age ggt eet ggg eta gte gge tge etg gee ggg Ala Pro Ser Pro Gly Ser Gly Pro Gly Leu Val Gly Cys Leu Ala Gly gaa cct gca ggc tcc cac agg aag agg tgt gga gac ctg ccc tcg ggg Glu Pro Ala Gly Ser His Arg Lys Arg Cys Gly Asp Leu Pro Ser Gly gcc tct ccc agg gtc cag cct gag ccc cca cca ggg gtc tct gcc cag Ala Ser Pro Arg Val Gln Pro Glu Pro Pro Pro Gly Val Ser Ala Gln cac agg aag ctg acc ctg gcc cag ctc tac cga atc agg acc acc ctg His Arg Lys Leu Thr Leu Ala Gln Leu Tyr Arg Ile Arg Thr Thr Leu ctg ctt aac tcc acg ctc act gcc tcg gag gtc tgagcagagg gaggccccca 3036 Leu Leu Asn Ser Thr Leu Thr Ala Ser Glu Val 

agagtgccat tgaccaagag acagcagaca gcctgcctcc tggggcgtgc cggcacctgc 3096 579/735

ttcagctact gcctcctgta tgcatgagcc ggatgctggg caggatccct gcctacgccc 3156
gggcccgatt tgcgctttgc cggactggat ggagtggagg aggcccaggc cacagtacca 3216
ccccacctgc ccaggcagcc cctcgtcacc tactccccga agttaccagc tcagctcgag 3276
tcttcagggc tgggctccta ggctgcccat cctacttcta ccctcactgg cctccagtgg 3336
gattcactcc tgccctgccc ccaccttccc agtcccacag gccacccctg gcttgggctg 3396
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<210> 156

<211> 912

<212> PRT

<213> Homo sapiens

<400> 156

Met Lys Lys Ser Leu Gly Glu Val Leu Leu Pro Val Phe Glu Arg

1 5 10 15

Lys Gly Ile Ala Leu Gly Lys Val Asp Ile Tyr Leu Asp Gln Ser Asn 20 25 30

Thr Pro Leu Ser Leu Thr Phe Glu Ala Tyr Arg Phe Gly Gly His Tyr
35 40 45

Leu		Val	Lys	Ala	Pro		Lys	Pro	Gly	Asp		Gly	Lys	Val	Glu
	50			٠		55					60				
G1n	Gly	Met	Lys	Asp	Ser	Lys	Ser	Leu	Ser	Leu	Pro	Ile	Leu	Arg	Pro
65					70					75					80
Ala	Gly	Thr	Gly	Pro	Pro	Ala	Leu	Glu	Arg	Val	Asp	Ala	G1n	Ser	Arg
				85					90					95	
Arg	Glu	Ser	Leu	Asp	Ile	Leu	Ala	Pro	Gly	Arg	Arg	Arg	Lys	Asn	Met
			100					105					110		
Ser	Glu	Phe	Leu	Gly	G1u	Ala	Ser	Ile	Pro	Gly	G1n	Glu	Pro	Pro	Thr
		115					120					125			
Pro	Ser	Ser	Cys	Ser	Leu	Pro	Ser	G1y	Ser	Ser	Gly	Ser	Thr	Asn	Thr
	130					135					140				
Gly	Asp	Ser	Trp	Lys	Asn	Arg	Ala	Ala	Ser	Arg	Phe	Ser	Gly	Phe	Phe
145					150					155					160
Ser	Ser	Gly	Pro	Ser	Thr	Ser	Ala	Phe	Gly	Arg	Glu	Val	Asp	Lys	Met
				165					170					175	
Glu	Gln	Leu	Glu	Gly	Lys	Leu	His	Thr	Tyr	Ser	Leu	Phe	Gly	Leu	Pro
			180					185					190		
Arg	Leu	Pro	Arg	Glv	Leu	Arg	Phe	Asp	His	Asp	Ser	Tro	Glu	Glu	Glu
_		195	J	•			200	-		-		205			

ſyr	Asp	Glu	Asp	Glu	Asp	Glu	Asp	Asn	Ala	Cys	Leu	Arg	Leu	Glu	Ası
	210					215					220				
Sor	Trn	Ara	G1 ₁₁	Leu	Tle	Asn	Glv	His	GI 11	I.vs	Len	Thr	Arø	Arø	Glr
	пр	1п. Р	014	Lou		пор	01,	1110	0.14		204	• • • • • • • • • • • • • • • • • • • •			
225					230					235					240
Cys	His	Gln	G1n	Glu	Ala	Val	Trp	Glu	Leu	Leu	His	Thr	Glu	Ala	Sea
				245					250					255	
			•												
rvr	Tle	Arø	I.vs	Leu	Arø	Val	Tle	Tle	Asn	Leu	Phe	Leu	Cvs	Cvs	Let
.,.	110	1111 6		Dou		,								-,-	
			260					265					270		
Leu	Asn	Leu	Gln	G1u	Ser	Gly	Leu	Leu	Cys	Glu	Val	Glu	Ala	G1u	Are
		275					280					285			
611	Phe	Ser	Asn	Ile	Pro	G111	Tle	Ala	G1n	Leu	His	Arg	Arg	Leu	Trr
bou		501	11011	110	110		110	11.2.0	<b></b>	200				20.	
	290					295					300				
Ala	Ser	Val	Met	Ala	Pro	Val	Leu	G1u	Lys	Ala	Arg	Arg	Thr	Arg	Ala
305					310					315					320
611	Len	Gln	Pro	Gly	Asn	Phe	Leu	Lvs	Gl v	Phe	Lvs	Met	Phe	G1 v	Sei
oou	Dou	0111	110		, iop	1110	Dou	_,,			~,~				
				325					330					335	
Leu	Phe	Lys	Pro	Tyr	Ile	Arg	Tyr	Cys	Met	Glu	Glu	Glu	Gly	Cys	Me
			340					345					350		

Glu Tyr Met Arg Gly Leu Leu Arg Asp Asn Asp Leu Phe Arg Ala Tyr

WO 02/053737			PCT/JP01/11389
355	360	365	

Ile Thr Trp Ala Glu Lys His Pro Gln Cys Gln Arg Leu Lys Leu Ser 

Asp Met Leu Ala Lys Pro His Gln Arg Leu Thr Lys Tyr Pro Leu Leu 

Leu Lys Ser Val Leu Arg Lys Thr Glu Glu Pro Arg Ala Lys Glu Ala 

Val Val Ala Met Ile Gly Ser Val Glu Arg Phe Ile His His Val Asn 

Ala Cys Met Arg Gln Arg Gln Glu Arg Gln Arg Leu Ala Ala Val Val 

Ser Arg Ile Asp Ala Tyr Glu Val Val Glu Ser Ser Ser Asp Glu Val 

Asp Lys Leu Leu Lys Glu Phe Leu His Leu Asp Leu Thr Ala Pro Ile 

Pro Gly Ala Ser Pro Glu Glu Thr Arg Gln Leu Leu Glu Gly Ser 

Leu Arg Met Lys Glu Gly Lys Asp Ser Lys Met Asp Val Tyr Cys Phe 

Leu Phe Thr Asp Leu Leu Leu Val Thr Lys Ala Val Lys Lys Ala Glu
515 520 525

Arg Thr Arg Val Ile Arg Pro Pro Leu Leu Val Asp Lys Ile Val Cys
530 535 540

Arg Glu Leu Arg Asp Pro Gly Ser Phe Leu Leu Ile Tyr Leu Asn Glu 545 550 555 560

Phe His Ser Ala Val Gly Ala Tyr Thr Phe Gln Ala Ser Gly Gln Ala 565 570 575

Leu Cys Arg Gly Trp Val Asp Thr Ile Tyr Asn Ala Gln Asn Gln Leu
580 585 590

Gln Gln Leu Arg Ala Gln Glu Pro Pro Gly Ser Gln Gln Pro Leu Gln
595 600 605

Glu Glu Glu Glu Glu Gly Glu Asp Ser Gly Thr Ser Ala Ala Ser Ser 625 630 635 640

Pro Thr Ile Met Arg Lys Ser Ser Gly Ser Pro Asp Ser Gln His Cys
645 650 655

Ala Ser Asp Gly Ser Thr Glu Thr Leu Ala Met Val Val Glu Pro
660 665 670
584/735

Gly Asp Thr Leu Ser Ser Pro Glu Phe Asp Ser Gly Pro Phe Ser Ser Gln Ser Asp Glu Thr Ser Leu Ser Thr Thr Ala Ser Ser Ala Thr Pro Thr Ser Glu Leu Leu Pro Leu Gly Pro Val Asp Gly Arg Ser Cys Ser Met Asp Ser Ala Tyr Gly Thr Leu Ser Pro Thr Ser Leu Gln Asp Phe Val Ala Pro Gly Pro Met Ala Glu Leu Val Pro Arg Ala Pro Glu Ser Pro Arg Val Pro Ser Pro Pro Pro Ser Pro Arg Leu Arg Arg Thr Pro Val Gln Leu Leu Ser Cys Pro Pro His Leu Leu Lys Ser Lys Ser Glu Ala Ser Leu Leu Gln Leu Leu Ala Gly Ala Gly Thr His Gly Thr Pro Ser Ala Pro Ser Arg Ser Leu Ser Glu Leu Cys Leu Ala Val Pro 

Ala Pro Gly Ile Arg Thr Gln Gly Ser Pro Gln Glu Ala Gly Pro Ser

820 825 830

Trp Asp Cys Arg Gly Ala Pro Ser Pro Gly Ser Gly Pro Gly Leu Val 835 840 845

Gly Cys Leu Ala Gly Glu Pro Ala Gly Ser His Arg Lys Arg Cys Gly 850 855 860

Asp Leu Pro Ser Gly Ala Ser Pro Arg Val Gln Pro Glu Pro Pro 865 870 875 880

Gly Val Ser Ala Gln His Arg Lys Leu Thr Leu Ala Gln Leu Tyr Arg 885 890 895

Ile Arg Thr Thr Leu Leu Leu Asn Ser Thr Leu Thr Ala Ser Glu Val
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<210> 157

<211> 3609

<212> DNA

<213> Homo sapiens

<220>

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<222> (152).. (3169)

<400> 157

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cgaggcctgt gacagca	agt tccacagcac	c atg cat t	at gat ggg cat g	tc 172
		Met His T	yr Asp Gly His V	al
		1	5	
		1.1 .11.		± 000
cgc ttc gac ctt cc				
Arg Phe Asp Leu Pr		Ser Val Leu		Ser
10	15		20	
acc cgg tca tgc cc	g ccg cgc acc	agc ccc gca	gtg gac ttg gag	gag 268
Thr Arg Ser Cys Pr	o Pro Arg Thr	Ser Pro Ala	Val Asp Leu Glu	Glu
25	30		35	
				•
gag gag gag gag ag	c tct gtg gat	ggc aaa ggg	gac cgg aag agc	aca 316
Glu Glu Glu Glu Se	r Ser Val Asp	Gly Lys Gly	Asp Arg Lys Ser	Thr
40	45	50		55
ggc ctg aaa ctc tc	c aag aag aaa	gca agg agg	aga cac acg gat	gac 364
Gly Leu Lys Leu Se	r Lys Lys Lys	Ala Arg Arg	Arg His Thr Asp	Asp
6	0	65	70	
cca agc aag gaa tg	c ttc act ctg	aaa ttt gac	ctg aat gtg gac	att 412
Pro Ser Lys Glu Cy				
75		80	85	
gag aca gag atc gt	c cca gcc atg	aag aag aag 587/735	tca ctg ggg gag	gtg 460

Glu	Thr	Glu	Ile	Val	Pro	Ala	Met	Lys	Lys	Lys	Ser	Leu	Gly	Glu	Val	
		90					95					100				
									-							
ctg	ctg	cct	gta	ttt	gaa	agg	aag	ggc	att	gcg	ctg	ggc	aaa	gtg	gac	508
Leu	Leu	Pro	Val	Phe	Glu	Arg	Lys	Gly	Ile	Ala	Leu	Gly	Lys	Val	Asp	
	105					110					115					
atc	tac	ctg	gac	cag	tcc	aac	aca	ccc	ctg	tcc	ctc	acc	ttc	gag	gcc	556
Ile	Tyr	Leu	Asp	Gln	Ser	Asn	Thr	Pro	Leu	Ser	Leu	Thr	Phe	Glu	Ala	
120					125					130					135	
								cgt								604
Tyr	Arg	Phe	Gly		His	Tyr	Leu	Arg		Lys	Ala	Pro	Ala		Pro	
				140					145					150		
								ggc								652
Gly	Asp	Glu		Lys	Val	Glu	Gin	Gly	Met	Lys	Asp	Ser		Ser	Leu	
			155					160					165			
																700
			•					ggg								700
ser	Leu	170	TIE	Leu	MIR	FIO	175	Gly	TILL	GIY	FIO	180	міа	Leu	GIU	
		110					175		•			100				
cat	ata		acc	cag	age	cac	caa	gag	age	cta	gac	atc	<b>+</b> +σ	acc	cct	748
								Glu								140
ия	185	пор	VIG	0111	501	190	111.6	014	501	Deu	195	110	Dou		110	
	100					100					100					
pac	CBC	CEC	CRC	ลลอ	aac	atø	t.cg	gag	tte	ct.ø	តិចិច	gSa	āca	agc	atc	796
								Glu								
оту	വദ	'm g	ın R	د ر ب	11311		JU1	588/		Dou	J13	J14		201		

200					205					210					215	
ccc	ggg	cag	gag	ccc	ccc	acg	ccc	tcc	agc	tgc	tct	ctg	ccc	agc	ggc	844
Pro	Gly	Gln	Glu	Pro	Pro	Thr	Pro	Ser	Ser	Cys	Ser	Leu	Pro	Ser	Gly	
				220					225					230		
agc	agt	ggc	agc	acc	aac	act	ggc	gac	agc	tgg	aag	aac	cgg	gcg	gcc	892
Ser	Ser	Gly	Ser	Thr	Asn	Thr	Gly	Asp	Ser	Trp	Lys	Asn	Arg	Ala	Ala	
			235					240					245	٠		
agt	cgc	ttc	agc	ggc	ttt	ttc	agc	tcc	ggc	ccc	agc	acc	agc	gcc	ttt	940
Ser	Arg	Phe	Ser	Gly	Phe	Phe	Ser	Ser	Gly	Pro	Ser	Thr	Ser	Ala	Phe	
		250					255					260				
ggc	cgg	gag	gta	gac	aag	atg	gag	cag	ctg	gag	ggc	aag	ctg	cac	acc	988
Gly	Arg	Glu	Val	Asp	Lys	Met	Glu	Gln	Leu	Glu	Gly	Lys	Leu	His	Thr	
	265					270					275					
tac	agc	ctc	ttc	ggg	ctg	ccc	agg	ctg	ccc	cgg	ggg	ctg	cgc	ttc	gac	1036
Tyr	Ser	Leu	Phe	Gly	Leu	Pro	Arg	Leu	Pro	Arg	Gly	Leu	Arg	Phe	Asp	
280					285					290					295	
cat	gac	tcc	tgg	gag	gag	gag	tac	gat	gaa	gac	gag	gat	gag	gac	aat	1084
His	Asp	Ser	Trp	Glu	Glu	Glu	Tyr	Asp	G1u	Asp	Glu	Asp	Glu	Asp	Asn	
				300					305					310		
gcc	tgc	ctg	agg	ctg	gag	gac	agc	tgg	cgg	gag	ctc	att	gat	ggg	cat	1132
Ala	Cys	Leu	Arg	Leu	Glu	Asp	Ser	Trp	Arg	Glu	Leu	Ile	Asp	G1y	His	
			315					320 589	735				325			

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gag	aag	ctg	acc	cgg	cgg	cag	tgc	cac	cag	cag	gag	gcg	gtg	tgg	gag	1180
Glu	Lys	Leu	Thr	Arg	Arg	Gln	Cys	His	Gln	G1n	Glu	Ala	Val	Trp	Glu	
		330					335					340				
ctg	ctg	cac	acg	gag	gcc	tcc	tac	atc	agg	aaa	ctg	cgg	gtg	atc	atc	1228
Leu	Leu	His	Thr	Glu	Ala	Ser	Tyr	Ile	Arg	Lys	Leu	Arg	Val	Ile	Ile	
	345					350					355					
aac	ctg	ttc	ctg	tgc	tgc	ctc	ctg	aac	ctg	caa	gag	tca	ggg	ctg	ctg	1276
Asn	Leu	Phe	Leu	Cys	Cys	Leu	Leu	Asn	Leu	G1n	Glu	Ser	Gly	Leu	Leu	
360					365					370					375	
								•								
tgt	gag	gtg	gag	gcg	gag	cgc	ctg	ttc	agc	aac	atc	ccg	gag	atc	gcg	1324
Cys	Glu	Val	Glu	Ala	Glu	Arg	Leu	Phe	Ser	Asn	Ile	Pro	Glu	Ile	Ala	
				380					385					390		
cag	ctg	cac	cgc	agg	ctg	tgg	gct	agc	gtg	atg	gcg	ccg	gtg	ctg	gag	1372
G1n	Leu	His	Arg	Arg	Leu	Trp	Ala	Ser	Val	Met	Ala	Pro	Val	Leu	Glu	
			395					400					405			
aag	gcg	cgg	cgc	acg	cga	gcg	ctg	cta	cag	ccc	ggg	gac	ttc	ctc	aaa	1420
Lys	Ala	Arg	Arg	Thr	Arg	Ala	Leu	Leu	Gln	Pro	Gly	Asp	Phe	Leu	Lys	
		410					415					420				
ggc	ttc	aag	atg	ttc	ggc	tcg	ctc	ttc	aag	ccc	tac	atc	cgc	tac	tgc	1468
Gly	Phe	Lys	Met	Phe	Gly	Ser	Leu	Phe	Lys	Pro	Tyr	Ile	Arg	Tyr	Cys	
	425					430					435					

atg gag gag gag ggc tgc atg gag tac atg cgc ggc ctg ctg cgc gac 1516

Met	Glu	Glu	Glu	Gly	Cys	Met	Glu	Tyr	Met	Arg	Gly	Leu	Leu	Arg	Asp	
440					445					450					455	
									,							1504
	_								tgg							1564
Asn	Asp	Leu	Phe	Arg	Ala	Tyr	Ile	Thr	Trp	Ala	Glu	Lys	His	Pro	Gln	
				460					465					470		
															•	
tgc	cag	agg	ctg	aag	ctg	agc	gac	atg	ctg	gcc	aaa	ccc	cac	cag	cgg	1612
Cys	Gln	Arg	Leu	Lys	Leu	Ser	Asp	Met	Leu	Ala	Lys	Pro	His	Gln	Arg	
			475					480					485			
ctc	acc	aag	tac	ccg	ctg	ctg	ctc	aag	tcg	gtg	ctg	agg	aag	acc	gag	1660
Leu	Thr	Lys	Tyr	Pro	Leu	Leu	Leu	Lys	Ser	Val	Leu	Arg	Lys	Thr	Glu	
		490					495					500				
gag	ccg	cgc	gcc	aag	gag	gcc	gtc	gtc	gcc	atg	atc	ggc	tcc	gtg	gag	1708
Glu	Pro	Arg	Ala	Lys	Glu	Ala	Val	Val	Ala	Met	Ile	Gly	Ser	Val	Glu	
	505					510					515					
cgc	ttc	atc	cac	cac	gtg	aac	gcg	tgc	atg	cgg	cag	cgg	cag	gag	cgg	1756
Arg	Phe	Ile	His	His	Val	Asn	Ala	Cys	Met	Arg	Gln	Arg	Gln	Glu	Arg	
520					525					530					535	
cao	caa	cta	aca	acc	a ta	ata	age	CEC	atc	gac	acc	tac	gag	øt.ø	øt.ø	1804
									Ile							1001
GIII	иц	Leu	AIA		Vai	141	ner	мg		nsp	nia	ıyı	GIU		141	
				540					545					550		
						_										1055
gaa	agc	agc	agc	gac	gaa	gtg	gac	aag 591/	ctc 735	ctg	aag	gaa	ttt	ctg	cac	1852
								J 21								

Glu Ser Ser Ser Asp Glu Val Asp Lys Leu Leu Lys Glu Phe Leu His ctg gac ttg aca gcg ccc atc cct ggc gcc tcc ccg gag gag acg cgg Leu Asp Leu Thr Ala Pro Ile Pro Gly Ala Ser Pro Glu Glu Thr Arg cag ctg ctg gag ggg agc ctg agg atg aag gag ggg aag gac agc Gln Leu Leu Glu Gly Ser Leu Arg Met Lys Glu Gly Lys Asp Ser aag atg gat gtg tac tgc ttc ctc ttc acg gat ctg ctg ttg gtg acc Lys Met Asp Val Tyr Cys Phe Leu Phe Thr Asp Leu Leu Val Thr aaa gca gtg aag aag gca gag agg acc agg gtc atc agg cca ccc ctg Lys Ala Val Lys Lys Ala Glu Arg Thr Arg Val Ile Arg Pro Pro Leu ctc gtg gac aag att gtg tgc cgg gag cta cgg gac cct ggg tcc ttc Leu Val Asp Lys Ile Val Cys Arg Glu Leu Arg Asp Pro Gly Ser Phe ctc ctt atc tac ctg aat gag ttt cac agt gct gta ggg gcc tac acg Leu Leu Ile Tyr Leu Asn Glu Phe His Ser Ala Val Gly Ala Tyr Thr ttc cag gcc agt ggc cag gcc ttg tgc cgt ggc tgg gtg gac acc att Phe Gln Ala Ser Gly Gln Ala Leu Cys Arg Gly Trp Val Asp Thr Ile 592/735

tac aat gcc cag aac cag ctg caa cag ctg cgt gca cag gag ccc cca Tyr Asn Ala Gln Asn Gln Leu Gln Gln Leu Arg Ala Gln Glu Pro Pro ggc agt cag cag ccc ctg cag agc ctg gaa gag gag gat gag cag Gly Ser Gln Gln Pro Leu Gln Ser Leu Glu Glu Glu Glu Asp Glu Gln ggc act tca gct gcc agc tcc cct acc atc atg cgg aaa agc agc ggc Gly Thr Ser Ala Ala Ser Ser Pro Thr Ile Met Arg Lys Ser Ser Gly age eec gae tet eag eac tgt gee tea gat gge tee aeg gag ace etg Ser Pro Asp Ser Gln His Cys Ala Ser Asp Gly Ser Thr Glu Thr Leu gcc atg gtt gtg gta gag cct ggg gac acg ctg tcc tcc ccc gag ttc Ala Met Val Val Val Glu Pro Gly Asp Thr Leu Ser Ser Pro Glu Phe gac agc ggt cct ttc agc tcc cag tct gat gag acc tct ctc agc acc 

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Asp Ser Gly Pro Phe Ser Ser Gln Ser Asp Glu Thr Ser Leu Ser Thr

act	gcc	tca	tct	gcc	acg	ccc	acc	agt	gag	ctg	ctg	ccc	ctg	ggt	ccg	2572
Thr	Ala	Ser	Ser	Ala	Thr	Pro	Thr	Ser	Glu	Leu	Leu	Pro	Leu	Gly	Pro	
			795					800					805			
gtg	gac	ggc	cgc	tcc	tgc	tcc	atg	gac	tct	gcc	tac	ggc	acc	ctc	tcc	2620
Val	Asp	Gly	Arg	Ser	Cys	Ser	Met	Asp	Ser	Ala	Tyr	Gly	Thr	Leu	Ser	
		810					815					820				
cca	acc	tcc	tta	caa	gac	ttt	gtg	gcc	cca	ggc	cca	atg	gca	gag	cta	2668
Pro	Thr	Ser	Leu	Gln	Asp	Phe	Val	Ala	Pro	G1y	Pro	Met	Ala	Glu	Leu	
	825					830					835					
gtg	cct	cgg	gcc	cca	gag	tcc	cca	cga	gtt	cct	tcc	cct	cca	ccc	tcg	2716
Val	Pro	Arg	Ala	Pro	G1u	Ser	Pro	Arg	Val	Pro	Ser	Pro	Pro	Pro	Ser	
840					845					850					855	
								•								
ccc	cgt	ctc	cgc	cgc	cgc	acc	cct	gtc	cag	ctg	ttg	agc	tgc	ccg	ccc	2764
Pro	Arg	Leu	Arg	Arg	Arg	Thr	Pro	Val	Gln	Leu	Leu	Ser	Cys	Pro	Pro	
				860					865					870		
														ctg		2812
His	Leu	Leu		Ser	Lys	Ser	Glu		Ser	Leu	Leu	Gln		Leu	Ala	
			875					880					885			
														ctg		2860
Gly	Ala		Thr	His	Gly	Thr		Ser	Ala	Pro	Ser		Ser	Leu	Ser	
		890					895					900				

gag ctc tgc	ctg gct gtt cc	a gcc cca ggt	att agg act cag ggc tco	2908
Glu Leu Cys	Leu Ala Val Pr	o Ala Pro Gly	Ile Arg Thr Gln Gly Sen	7
905	91	)	915	
cct cag gaa	gct ggg ccc ag	c tgg gat tgc	cga ggg gcc cct agc cct	2956
Pro Gln Glu	Ala Gly Pro Se	Trp Asp Cys	Arg Gly Ala Pro Ser Pro	<b>)</b>
920	925		930 935	5
ggc agc ggt	cct ggg cta gt	ggc tgc ctg	gcc ggg gaa cct gca ggc	3004
Gly Ser Gly	Pro Gly Leu Va	l Gly Cys Leu	Ala Gly Glu Pro Ala Gly	7
	940	945	950	
tcc cac agg	aag agg tgt gg	a gac ctg ccc	tcg ggg gcc tct ccc agg	3052
Ser His Arg	Lys Arg Cys Gl	Asp Leu Pro	Ser Gly Ala Ser Pro Arg	5
	955	960	965	
	•			
gtc cag cct	gag ccc cca cca	a ggg gtc tct	gcc cag cac agg aag ctg	3100
Val Gln Pro	Glu Pro Pro Pro	o Gly Val Ser	Ala Gln His Arg Lys Leu	ı
970		975	980	
acc ctg gcc	cag ctc tac cga	a atc agg acc	acc ctg ctg ctt aac tcc	3148
Thr Leu Ala	Gln Leu Tyr Ar	g Ile Arg Thr	Thr Leu Leu Leu Asn Ser	•
985	990	)	995	
			gaggccccca agagtgccat	3199
	Ala Ser Glu Va	l		
1000	1005			

tgaccaagag acagcagaca gcctgcctcc tggggcgtgc cggcacctgc ttcagctact 3259 595/735

gentectifia tigeatigate ggatigatigg caggatecet gentaciene gggecegati 3319

tigegettige eggactigat ggagtigagg aggeceagge cacagitacea ecceacetige 3379

ceaggeagee ectegicace tacteecega agitaceage teagetegag tetteaggee 3439

tigegeteeta ggetigeeeat ectaciteta eccetacitig ectecagiig gaiteaetee 3499

tigeeetigee ecacetteee agiteeeaag geeaeeeetig getitiggetig ggitetigia 3559

agitacitat tiattigaget titiggitett tiataaagae tigeetagae 3609

<210> 158

<211> 1006

<212> PRT

<213> Homo sapiens

<400> 158

Met His Tyr Asp Gly His Val Arg Phe Asp Leu Pro Pro Gln Gly Ser

1 5 10 15

Val Leu Ala Arg Asn Val Ser Thr Arg Ser Cys Pro Pro Arg Thr Ser
20 25 30

Pro Ala Val Asp Leu Glu Glu Glu Glu Glu Glu Ser Ser Val Asp Gly
35 40 45

Lys	Gly	Asp	Arg	Lys	Ser	Thr	Gly	Leu	Lys	Leu	Ser	Lys	Lys	Lys	Ala
	50					55					60				
Arg	Arø	Arg	His	Thr	Asn	Asp	Pro	Ser	I.vs	Glu	Cvs	Phe	Thr	Leu	l.vs
					70	,			-,-	75	-,-				
65					70					73					80
Phe	Asp	Leu	Asn	Val	Asp	Ile	Glu	Thr	Glu	Ile	Val	Pro	Ala	Met	Lys
				85					90					95	
Lys	Lys	Ser	Leu	Gly	Glu	Val	Leu	Leu	Pro	Val	Phe	Glu	Arg	Lys	Gly
			100					105					110		
		•													
Ile	Ala	Leu	G1v	Lvs	Val	Asp	Ile	Tvr	Leu	Asp	G1n	Ser	Asn	Thr	Pro
		115	,				120	-,-				125			
		110					120					120			
	•		æ1	<b>5</b> 1	0.1	4.3	<b></b>		DI	<b>63</b>	01		<b></b>		
Leu		Leu	ınr	Pne	GIU	Ala	ıyr	Arg	Pne	GIÀ		HIS	lyr	Leu	Arg
	130					135					140				
Val	Lys	Ala	Pro	Ala	Lys	Pro	Gly	Asp	Glu	Gly	Lys	Val	Glu	Gln	Gly
145					150					155					160
Met	Lys	Asp	Ser	Lys	Ser	Leu	Ser	Leu	Pro	Ile	Leu	Arg	Pro	Ala	Gly
				165					170					175	
Th	C1	Dec	Dro	۸1	I ~··	C1	۸	Vo 1	۸	41.	C1-	C	۸	A	C1
HIL	ΩŢÃ	rro		ита	Leu	G1u	wrg		лsp	ATS	GIU	ser		vr.g	gru
			180					185					190		
Ser	Leu	Asp	Ile	Leu	Ala	Pro	Gly	Arg	Arg	Arg	Lys	Asn	Met	Ser	Glu

200

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205

195

•															
Phe	Leu	Gly	Glu	Ala	Ser	Ile	Pro	Gly	G1n	Glu	Pro	Pro	Thr	Pro	Ser
	210					215					220				
				ı											
Ser	Cys	Ser	Leu	Pro	Ser	Gly	Ser	Ser	Gly	Ser	Thr	Asn	Thr	Gly	Asp
225			•		230					235					240
Ser	Trp	Lys	Asn	Arg	Ala	Ala	Ser	Arg	Phe	Ser	G1y	Phe	Phe	Ser	Ser
				245					250					255	
Gly	Pro	Ser	Thr	Ser	Ala	Phe	Gly	Arg	Glu	Val	Asp	Lys	Met	Glu	Gln
			260					265					270		
Leu	Glu	Gly	Lys	Leu	His	Thr	Tyr	Ser	Leu	Phe	Gly	Leu	Pro	Arg	Leu
		275					280					285			
Pro	Arg	Gly	Leu	Arg	Phe	Asp	His	Asp	Ser	Trp	Glu	Glu	Glu	Tyr	Asp
	290					295					300				
Glu	Asp	Glu	Asp	Glu	Asp	Asn	Ala	Cys	Leu	Arg	Leu	Glu	Asp	Ser	Trp
305					310					315					320
Arg	Glu	Leu	Ile	Asp	Gly	His	G1u	Lys	Leu	Thr	Arg	Arg	Gln	Cys	His
				325					330					335	
Gln	G1n	Glu	Ala	Val	Trp	G1u	Leu	Leu	His	Thr	Glu	Ala	Ser	Tyr	Ile
			340					345					350		

Arg Lys Leu Arg Val Ile Ile Asn Leu Phe Leu Cys Cys Leu Leu Asn

W	O 02/	0537	37												PCT/JP01/11389
	•	355					360					365			
Leu	G1n 370	Glu	Ser	Gly	Leu	Leu 375	Cys	Glu	Val	Glu	Ala 380	G1u	Arg	Leu	Phe
Ser 385	Asn	Ile	Pro	Glu	Ile 390	Ala	Gln	Leu	His	Arg 395	Arg	Leu	Trp	Ala	Ser 400
Val	Met	Ala	Pro	Val 405	Leu	Glu	Lys	Ala	Arg 410	Arg	Thr	Arg	Ala	Leu 415	Leu
Gln	Pro	Gly	Asp 420	Phe	Leu	Lys	Gly	Phe 425	Lys	Met	Phe	G1y	Ser 430	Leu	Phe
Lys	Pro	Tyr 435	Ile	Arg	Tyr	Cys	Met 440	G1u	Glu	Glu	Gly	Cys 445	Met	G1u	Tyr
Met	Arg	Gly	Leu	Leu	Arg	Asp	Asn	Asp	Leu	Phe	Arg	Ala	Tyr	Ile	Thr

Trp Ala Glu Lys His Pro Gln Cys Gln Arg Leu Lys Leu Ser Asp Met
465 470 475 480

460

455

450

Leu Ala Lys Pro His Gln Arg Leu Thr Lys Tyr Pro Leu Leu Lys
485 490 495

Ser Val Leu Arg Lys Thr Glu Glu Pro Arg Ala Lys Glu Ala Val Val
500 505 510

Ala	Met	Ile 515	Gly	Ser	Val	Glu	Arg 520	Phe	Ile	His	His	Val 525	Asn	Ala	Cys
Met	Arg 530	Gln	Arg	Gln	Glu	Arg 535	Gln	Arg	Leu	Ala	Ala 540	Val	Val	Ser	Arg
Ile 545	Asp	Ala	Tyr	Glu	Val 550	Val	Glu	Ser	Ser	Ser 555	Asp	Glu	Val	Asp	Lys 560
Leu	Leu	Lys	Glu	Phe 565	Leu	His	Leu	Asp	Leu 570	Thr	Ala	Pro	Ile	Pro 575	Gly
Ala	Ser	Pro	G1u 580	Glu	Thr	Arg	Gln	Leu 585	Leu	L _{eu}	Glu	G1y	Ser 590	Leu	Arg
Met	Lys	G1u 595	G1y	Lys	Asp	Ser	Lys 600	Met	Asp	Val	Tyr	Cys 605	Phe	Leu	Pḥe
Thr	Asp 610	Leu	Leu	Leu	Val	Thr 615	Lys	Ala	Val	Lys	Lys 620	Ala	G1u	Arg	Thr
Arg 625	Val	Ile	Arg	Pro	Pro 630	Leu	Leu	Val	Asp	Lys 635	Ile	Val	Cys	Arg	Glu 640
Leu	Arg	Asp	Pro	Gly 645	Ser	Phe	Leu	Leu	Ile 650	Tyr	Leu	Asn	Glu	Phe 655	His

Ser Ala Val Gly Ala Tyr Thr Phe Gln Ala Ser Gly Gln Ala Leu Cys

665

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670

660

Ala	Met	Ile	Gly	Ser	Val	Glu	Arg	Phe	Ile	His	His	Val	Asn	Ala	Cys
		515					520					525			
Met	Arg	Gln	Arg	G1n	G1u	Arg	G1n	Arg	Leu	Ala	Ala	Val	Val	Ser	Arg
	530		0			535		0			540				0
	550					000					J40				
Ile	Asp	Ala	Tyr	Glu	Val	Val	G1u	Ser	Ser	Ser	Asp	Glu	Val	Asp	Lys
545					550					555					560
Leu	Leu	Lvs	G1u	Phe	Leu	His	Leu	Asp	Leu	Thr	Ala	Pro	Ile	Pro	Glv
				565					570					575	
				505					310					313	
Ala	Ser	Pro	Glu	Glu	Thr	Arg	Gln	Leu	Leu	Leu	Glu	Gly	Ser	Leu	Arg
			580					585					590		
Met	Lys	G111	Gl v	Lvs	Asp	Ser	Lvs	Met	Asp	Val	Tvr	Cvs	Phe	Len	Phe
	2,0		01,	2,0	пор	501				, 01	-,-		1110	Dou	1 110
		595					600					605			
Thr	Asp	Leu	Leu	Leu	Val	Thr	Lys	Ala	Val	Lys	Lys	Ala	G1u	Arg	${\tt Thr}$

Arg Val Ile Arg Pro Pro Leu Leu Val Asp Lys Ile Val Cys Arg Glu

620

640

635

615

630

610

625

Leu Arg Asp Pro Gly Ser Phe Leu Leu Ile Tyr Leu Asn Glu Phe His
645 650 655

Ser Ala Val Gly Ala Tyr Thr Phe Gln Ala Ser Gly Gln Ala Leu Cys 660 665 670 600/735

Arg	Gly	Trp	Val	Asp	Thr	Ile	Tyr	Asn	Ala	Gln	Asn	G1n	Leu	Gln	Gln
		675					680					685			
Leu	Arg	Ala	Gln	Glu	Pro	Pro	Gly	Ser	G1n	G1n	Pro	Leu	Gln	Ser	Leu
	690					695					700				
Glu	Glu	Glu	G1u	Asp	Glu	Gln	Glu								
705					710					715					720
Glu	Glu	Glu	Gly	Glu	Asp	Ser	Gly	Thr	Ser	Ala	Ala	Ser	Ser	Pro	Thr
				725					730					735	
Ile	Met	Arg	Lys	Ser	Ser	G1y	Ser	Pro	Asp	Ser	Gln	His	Cys	Ala	Ser
			740					745					750		
Asp	Gly	Ser	Thr	Glu	Thr	Leu	Ala	Met	Val	Val	Val	Glu	Pro	Gly	Asp
		755					760					765			
Thr	Leu	Ser	Ser	Pro	Glu	Phe	Asp	Ser	Gly	Pro	Phe	Ser	Ser	G1n	Ser
	770					775					780				
Asp	Glu	Thr	Ser	Leu	Ser	Thr	Thr	Ala	Ser	Ser	Ala	Thr	Pro	Thr	Ser
785					790					795					800
Glu	Leu	Leu	Pro	Leu	Gly	Pro	Val	Asp	Gly	Arg	Ser	Cys	Ser	Met	Asp

Ser Ala Tyr Gly Thr Leu Ser Pro Thr Ser Leu Gln Asp Phe Val Ala 601/735

805

810

815

820 825 830

Pro Gly Pro Met Ala Glu Leu Val Pro Arg Ala Pro Glu Ser Pro Arg 835 840 845

Val Pro Ser Pro Pro Pro Ser Pro Arg Leu Arg Arg Arg Thr Pro Val 850 855 860

Gln Leu Leu Ser Cys Pro Pro His Leu Leu Lys Ser Lys Ser Glu Ala 865 870 875 880

Ser Leu Leu Gln Leu Leu Ala Gly Ala Gly Thr His Gly Thr Pro Ser 885 890 895

Ala Pro Ser Arg Ser Leu Ser Glu Leu Cys Leu Ala Val Pro Ala Pro 900 905 910

Gly Ile Arg Thr Gln Gly Ser Pro Gln Glu Ala Gly Pro Ser Trp Asp 915 920 925

Cys Arg Gly Ala Pro Ser Pro Gly Ser Gly Pro Gly Leu Val Gly Cys 930 935 940

Leu Ala Gly Glu Pro Ala Gly Ser His Arg Lys Arg Cys Gly Asp Leu 945 950 955 960

Pro Ser Gly Ala Ser Pro Arg Val Gln Pro Glu Pro Pro Pro Gly Val 965 970 975

Ser Ala Gln His Arg Lys Leu Thr Leu Ala Gln Leu Tyr Arg Ile Arg 980 985 990

Thr Thr Leu Leu Leu Asn Ser Thr Leu Thr Ala Ser Glu Val
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<222> (93).. (3089)

**<400> 159** 

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gct aga ggc cag tcc caa agt ctc cag gca tca ggg ctg cag ccc agg 161
Ala Arg Gly Gln Ser Gln Ser Leu Gln Ala Ser Gly Leu Gln Pro Arg

10 15 20

age etc aag geg gee egg geg act gga egg eeg gae agg tee ega 209 603/735

Ser	Leu	Lys	Ala	Ala	Arg	Arg	Ala	Thr	Gly	Arg	Pro	Asp	Arg	Ser	Arg	
	25					30					35					
gca	gcc	ccg	ccc	aac	atg	gac	cca	gac	ccc	cag	gcg	ggc	gtg	cag	gtg	257
Ala	Ala	Pro	Pro	Asn	Met	Asp	Pro	Asp	Pro	Gln	Ala	Gly	Val	G1n	Val	
40					45					50					55	
ggc	atg	cgg	gtg	gtg	cgc	ggc	gtg	gac	tgg	aag	tgg	ggc	cag	cag	gac	305
Gly	Met	Arg	Val	Val	Arg	Gly	Val	Asp	Trp	Lys	Trp	Gly	Gln	Gln	Asp	
				60					65					70		
ggc	ggc	gag	ggc	ggc	gtg	ggc	acg	gtg	gtg	gag	ctt	ggc	cgc	cac	ggc	353
G1y	G1y	Glu	Gly	Gly	Val	Gly	Thr	Val	Val	Glu	Leu	Gly	Arg	His	Gly	
			75					80					85			
											•					
agc	ссс	tcg	aca	ссс	gac	cgc	aca	gtg	gtc	gtg	cag	tgg	gac	cag	ggc	401
Ser	Pro	Ser	Thr	Pro	Asp	Arg	Thr	Val	Val	Val	Gln	Trp	Asp	Gln	Gly	
		90					95					100				
acg	cgc	acc	aac	tac	cgc	gcc	ggc	tac	cag	ggc	gcg	cac	gac	ctg	ctg	449
Thr	Arg	Thr	Asn	Tyr	Arg	Ala	Gly	Tyr	G1n	Gly	Ala	His	Asp	Leu	Leu	
	105					110					115					
ctg	tac	gac	aac	gcc	cag	atc	ggc	gtc	cgg	cac	ccc	aac	atc	atc	tgt	497
Leu	Tyr	Asp	Asn	Ala	Gln	Ile	Gly	Val	Arg	His	Pro	Asn	Ile	Ile	Cys	
120					125					130					135	
gac	tgc	tgc	aag	aag	cac	ggg	ctg	cgg	ggg	atg	cgc	tgg	aag	tgc	cgt	545
Asp	Cys	Cys	Lys	Lys	His	Gly	Leu	Arg	Gly	Met	Arg	Trp	Lys	Cys	Arg	

gtg tgc ctg gac tac gac ctc tgc acg cag tgc tac atg cac aac aag Val Cys Leu Asp Tyr Asp Leu Cys Thr Gln Cys Tyr Met His Asn Lys cat gag ctc gcc cac gcc ttc gac cgc tac gag acc gct cac tcg cgc His Glu Leu Ala His Ala Phe Asp Arg Tyr Glu Thr Ala His Ser Arg cct gtc aca ctg agt ccc cgc cag ggc ctc ccg agg atc cca cta agg Pro Val Thr Leu Ser Pro Arg Gln Gly Leu Pro Arg Ile Pro Leu Arg ggc atc ttc cag gga gcg aag gtg gtg cga ggc ccc ttc tgg gag tgg Gly Ile Phe Gln Gly Ala Lys Val Val Arg Gly Pro Phe Trp Glu Trp ggc tca cag gat gga ggg gaa ggg aaa ccg ggc cgt gtg gtg gac atc Gly Ser Gln Asp Gly Gly Glu Gly Lys Pro Gly Arg Val Val Asp Ile cgt ggc tgg gat gtg gag aca ggc cgg agt gtg gcc agc gtg acg tgg Arg Gly Trp Asp Val Glu Thr Gly Arg Ser Val Ala Ser Val Thr Trp 

> 255 260 605/735

gct gat ggt acc acc aat gtg tac cgt gtg ggc cac aag ggc aag gtg

Ala Asp Gly Thr Thr Asn Val Tyr Arg Val Gly His Lys Gly Lys Val

gac	ctc	aag	tgt	gtg	ggc	gag	gca	gcg	ggc	ggc	ttc	tac	tac	aag	gac	929
Asp	Leu	Lys	Cys	Val	Gly	G1u	Ala	Ala	Gly	G1y	Phe	Tyr	Tyr	Lys	Asp	
	265					270					275					
cac	ctc	cca	agg	ctc	ggc	aag	ccg	gcg	gag	ctg	cag	cgc	agg	gtg	agt	977
His	Leu	Pro	Arg	Leu	Gly	Lys	Pro	Ala	Glu	Leu	Gln	Arg	Arg	Val	Ser	
280					285					290					295	
gct	gac	agc	cag	ссс	ttc	cag	cac	ggg	gac	aag	gtc	aag	tgt	ctg	ctg	1025
Ala	Asp	Ser	Gln	Pro	Phe	Gln	His	Gly	Asp	Lys	Val	Lys	Cys	Leu	Leu	
				300					305					310		
gac	act	gat	gtc	ctg	cgg	gag	atg	cag	gaa	ggc	cac	ggc	ggc	tgg	aac	1073
Asp	Thr	Asp	Val	Leu	Arg	Glu	Met	G1n	Glu	Gly	His	G1y	Gly	Trp	Asn	
			315					320					325			
ccc	agg	atg	gcg	gag	ttt	atc	gga	cag	acg	ggc	acc	gtg	cat	cgt	atc	1121
Pro	Arg	Met	Ala	G1u	Phe	Ile	Gly	Gln	Thr	Gly	Thr	Val	His	Arg	Ile	
		330					335					340				
acg	gac	cgc	ggg	gac	gtg	cgc	gtg	cag	ttc'	aac	cac	gag	acg	cgc	tgg	1169
Thr	Asp	Arg	G1y	Asp	Val	Arg	Val	Gln	Phe	Asn	His	G1u	Thr	Arg	Trp	
	345					350					355					
		-														
acc	ttc	cac	ccc	ggg	gcg	ctc	acc	aag	cac	cac	tcc	ttc	tgg	gtg	ggc	1217
					Ala											•
360				-	365					370			_		375	

gac	gtg	gtc	cgg	gtc	atc	ggc	gac	ctt	gac	aca	gtg	aag	cgg	ctg	cag	1265
Asp	Val	Val	Arg	Val	Ile	Gly	Asp	Leu	Asp	Thr	Val	Lys	Arg	Leu	Gln	
				380					385					390		
gct	ggg	cat	ggc	gag	tgg	acg	gac	gac	atg	gcc	cct	gcc	ctg	ggc	cgc	1313
Ala	Gly	His	Gly	Glu	Trp	Thr	Asp	Asp	Met	Ala	Pro	Ala	Leu	Gly	Arg	
			395					400					405			
					_											
gtc	ggg	aag	gtg	gtg	aaa	gtg	ttt	gga	gac	ggg	aac	ctg	cgt	gta	gca	1361
Val	Gly	Lys	Val	Val	Lys	Val	Phe	Gly	Asp	Gly	Asn	Leu	Arg	Val	Ala	
		410					415					420				
gtc	gct	ggt	cag	cgg	tgg	acc	ttc	agc	ccc	tcc	tgc	ctg	gtg	gcc	tac	1409
Val	Ala	G1y	Gln	Arg	Trp	Thr	Phe	Ser	Pro	Ser	Cys	Leu	Val	Ala	Tyr	
	425					430					435					
cgg	ccc	gag	gag	gat	gcc	aac	ctg	gac	gtg	gcc	gag	cgc	gcc	cgg	gag	1457
Arg	Pro	Glu	Glu	Asp	Ala	Asn	Leu	Asp	Val	Ala	Glu	Arg	Ala	Arg	Glu	
440					445					450					455	
aac	aaa	agc	tca	ctg	agc	gtg	gcc	ctg	gac	aag	ctt	cgg	gcc	cag	aag	1505
Asn	Lys	Ser	Ser	Leu	Ser	Val	Ala	Leu	Asp	Lys	Leu	Arg	Ala	Gln	Lys	
				460					465					470		
agt	gac	cca	gag	cac	ccg	gga	agg	ctg	gtg	gtg	gag	gtg	gcg	ctg	ggt	1553
Ser	Asp	Pro	Glu	His	Pro	Gly	Arg	Leu	Val	Val	Glu	Val	Ala	Leu	Gly	
			475					480					485			
aac	gca	gcc	cgg	gct	ctg	gac	ctg	ctg 607/		agg	cgc	cca	gag	caa	gtg	1601
								UU //	, ,,,							

Asn Ala Ala Arg Ala Leu Asp Leu Leu Arg Arg Arg Pro Glu Gln Val gac acc aag aac caa ggc agg acc gct ctg caa gtg gct gcc tac ctg Asp Thr Lys Asn Gln Gly Arg Thr Ala Leu Gln Val Ala Ala Tyr Leu ggc cag gtg gag ttg ata cgg ctg cta caa gcc agg gcg ggc gtg Gly Gln Val Glu Leu Ile Arg Leu Leu Cln Ala Arg Ala Gly Val gac ctg ccg gac gac gag ggc aac acg gca ctg cac tac gcg gcc ctg Asp Leu Pro Asp Asp Glu Gly Asn Thr Ala Leu His Tyr Ala Ala Leu ggg aac cag ccc gag gcc acc agg gtg ctc ctg agt gct ggg tgc cgg Gly Asn Gln Pro Glu Ala Thr Arg Val Leu Leu Ser Ala Gly Cys Arg gcg gac gcc atc aac agc acc cag agc aca gca ctg cac gtg gcc gtg Ala Asp Ala Ile Asn Ser Thr Gln Ser Thr Ala Leu His Val Ala Val cag agg ggc ttc ctg gag gtg gtg cgg gcc ctg tgt gag cgc ggc tgt Gln Arg Gly Phe Leu Glu Val Val Arg Ala Leu Cys Glu Arg Gly Cys gac gtc aac ctg ccc gac gcc cac tcg gac acg ccc ctg cac tcc gcc Asp Val Asn Leu Pro Asp Ala His Ser Asp Thr Pro Leu His Ser Ala 608/735

W	/ <b>O</b> 02	/0537	37												PCT/J	P01/11389
600					605					610					615	
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Ile	Ser	Ala	Gly	Thr	Gly	Ala	Ser	Gly	Ile	Val	Glu	Val	Leu	Thr	Glu	
				620					625					630		
					gtt										_	2033
Val	Pro	Asn		Asp	Val	Thr	Ala		Asn	Ser	GIn	Gly			Leu	
			635					640					645			
ctg	cac	cat	gcc	tcc	ctc	aag	ggt	cac	gcg	cta	gct	gtg	aga	aag	att	2081
					Leu											
		650					655					660	_			
																•
ctg	gct	cgg	gcg	cgg	cag	ctg	gtg	gac	gcc	aag	aag	gag	gac	ggc	ttc	2129
Leu	Ala	Arg	Ala	Arg	Gln	Leu	Val	Asp	Ala	Lys	Lys	G1u	Asp	G1y	Phe	
	665					670					675					
					gct											2177
	Ala	Leu	His	Leu	Ala	Ala	Leu	Asn	Asn		Arg	Glu	Val	Ala		
680					685					690					695	
atc	ctc	atc	cgg	gag	ggc	cgc	tgt	gac	gtg	aac	gtg	cgc	aac	Cgg	aag ·	2225
					Gly										_	2220
				700	•	_	·	-	705					710	•	
ctg	cag	tcc	ccg	ctg	cat	ctc	gcc	gtg	caa	cag	gcc	cac	gtg	ggg	ctg	2273
Leu	Gln	Ser	Pro	Leu	His	Leu	Ala	Val	Gln	Gln	Ala	His	Val	Gly	Leu	
			715					720					725			

gtg	ccg	cta	ctg	gtg	gac	gct	ggg	tgc	agt	gtc	aac	gcc	gag	gac	gag	2321
Val	Pro	Leu	Leu	Val	Asp	Ala	G1y	Cys	Ser	Val	Asn	Ala	Glu	Asp	Glu	
		730					735					740				
gag	ggg	gac	aca	gcc	ctg	cac	gtg	gcg	ctg	cag	cgt	cat	cag	ctg	ctg	2369
Glu	Gly	Asp	Thr	Ala	Leu	His	Val	Ala	Leu	Gln	Arg	His	Gln	Leu	Leu	
	745					750					755					
ccc	ctg	gtg	gct	gat	ggg	gcc	ggg	ggg	gac	cca	ggg	ccc	ttg	cag	ctg	2417
Pro	Leu	Val	Ala	Asp	Gly	Ala	Gly	Gly	Asp	Pro	Gly	Pro	Leu	Gln	Leu	
760					765					770					775	
ctg	tcc	agg	cta	cag	gcc	tcg	ggc	ctc	ccc	ggc	agc	gcg	gag	ctg	acg	2465
Leu	Ser	Arg	Leu	G1n	Ala	Ser	Gly	Leu	Pro	G1y	Ser	Ala	Glu	Leu	Thr	
				780					785					790		
gtg	ggc	gcg	gcg	gtc	gcc	tgc	ttc	ctg	gcg	ctg	gag	ggc	gcc	gac	gtg	2513
Va1	G1y	Ala	Ala	Val	Ala	Cys	Phe	Leu	Ala	Leu	Glu	Gly	Ala	Asp	Val	
			795					800					805			
agc	tac	acc	aac	cac	cgc	ggt	cgg	agc	ccg	ctg	gac	ctg	gcc	gcc	gag	2561
Ser	Tyr	Thr	Asn	His	Arg	Gly	Arg	Ser	Pro	Leu	Asp	Leu	Ala	Ala	Glu	
		810					815					820				
ggt	cgc	gtg	ctc	aag	gcc	ctt	cag	ggc	tgc	gcc	cag	cgc	ttc	cgg	gag	2609
G1y	Arg	Val	Leu	Lys	Ala	Leu	G1n	Gly	Cys	Ala	Gln	Arg	Phe	Arg	Glu	
	825					830					835					

cgg	cag	gcg	ggc	ggg	ggc	gcg	gcc	ccg	ggc	ccc	agg	caa	acg	ctc	ggg	2657
Arg	Gln	Ala	G1y	Gly	Gly	Ala	Ala	Pro	Gly	Pro	Arg	Gln	Thr	Leu	Gly	
840		•			845					850				•	855	
acc	ccc	aac	acc	gtg	acg	aac	ctg	cac	gtg	ggc	gcc	gcg	ccg	ggg	ccc	2705
Thr	Pro	Asn	Thr	Val	Thr	Asn	Leu	Ĥis	Val	Gly	Ala	Ala	Pro	Gly	Pro	
				860					865					870		
gag	gcc	gct	gag	tgc	ctg	gtg	tgc	tcc	gag	ctg	gcg	ctg	ctg	gtg	ctg	2753
Glu	Ala	Ala	Glu	Cys	Leu	Val	Cys	Ser	Glu	Leu	Ala	Leu	Leu	Val	Leu	
			875					880					885			
ttc	tcg	ccg	tgc	cag	cac	cgc	acc	gtg	tgt	gag	gag	tgc	gcg	cgc	agg	2801
Phe	Ser	Pro	Cys	Gln	His	Arg	Thr	Val	Cys	Glu	G1u	Cys	Ala	Arg	Arg	
		890					895					900				
atg	aag	aag	tgc	atc	agg	tgc	cag	gtg	gtc	gtc	agc	aag	aaa	ctg	cgc	2849
Met	Lys	Lys	Cys	Ile	Arg	Cys	Gln	Val	Val	Val	Ser	Lys	Lys	Leu	Arg	
	905					910					915					
cca	gac	ggc	tct	gag	gtg	gcg	agc	gcc	gcc	ccc	gcc	ccc	ggc	ccg	ccg	2897
Pro	Asp	Gly	Ser	Glu	Val	Ala	Ser	Ala	Ala	Pro	Ala	Pro	Gly	Pro	Pro	
920					925					930					935	
cgc	cag	ctg	gtg	gag	gag	ctg	cag	agc	cgc	tac	cgg	cag	atg	gag	gaa	2945
Arg	Gln	Leu	Val	Glu	Glu	Leu	G1n	Ser	Arg	Tyr	Arg	Gln	Met	Glu	Glu	
				940					945					950		
cgc	atc	acc	tgc	ccc	atc	tgc	atc	_		cac	atc	cgc	ctc	gtg	ttc	2993
								611/	133							

Arg Ile Thr Cys Pro Ile Cys Ile Asp Arg His Ile Arg Leu Val Phe 955 960 965

cag tgc ggc cac ggc gca tgc gcc ccc tgc ggc tcc gcg ctc agc gcc 3041

Gln Cys Gly His Gly Ala Cys Ala Pro Cys Gly Ser Ala Leu Ser Ala

970 975 980

tgc ccc atc tgc cgc cag ccc atc cgc gac cgc atc cag atc ttc gtg 3089

Cys Pro Ile Cys Arg Gln Pro Ile Arg Asp Arg Ile Gln Ile Phe Val

985 990 995

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<212> PRT

<213> Homo sapiens

<400> 160

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1 5 10 15

Ala Ser Gly Leu Gln Pro Arg Ser Leu Lys Ala Ala Arg Arg Ala Thr
20 25 30

Gly Arg Pro Asp Arg Ser Arg Ala Ala Pro Pro Asn Met Asp Pro Asp 612/735

35 · 40 45

Pro Gln Ala Gly Val Gln Val Gly Met Arg Val Val Arg Gly Val Asp
50 55 60

Trp Lys Trp Gly Gln Gln Asp Gly Glu Gly Gly Val Gly Thr Val
65 70 75 80

Val Glu Leu Gly Arg His Gly Ser Pro Ser Thr Pro Asp Arg Thr Val

85 90 95

Val Val Gln Trp Asp Gln Gly Thr Arg Thr Asn Tyr Arg Ala Gly Tyr
100 105 110

Gln Gly Ala His Asp Leu Leu Leu Tyr Asp Asn Ala Gln Ile Gly Val 115 120 125

Arg His Pro Asn Ile Ile Cys Asp Cys Cys Lys Lys His Gly Leu Arg 130 135 140

Gly Met Arg Trp Lys Cys Arg Val Cys Leu Asp Tyr Asp Leu Cys Thr 145 150 155 160

Gln Cys Tyr Met His Asn Lys His Glu Leu Ala His Ala Phe Asp Arg 165 170 175

Tyr Glu Thr Ala His Ser Arg Pro Val Thr Leu Ser Pro Arg Gln Gly
180 185 190

Leu Pro Arg Ile Pro Leu Arg Gly Ile Phe Gln Gly Ala Lys Val Val Arg Gly Pro Phe Trp Glu Trp Gly Ser Gln Asp Gly Gly Glu Gly Lys Pro Gly Arg Val Val Asp Ile Arg Gly Trp Asp Val Glu Thr Gly Arg Ser Val Ala Ser Val Thr Trp Ala Asp Gly Thr Thr Asn Val Tyr Arg Val Gly His Lys Gly Lys Val Asp Leu Lys Cys Val Gly Glu Ala Ala Gly Gly Phe Tyr Tyr Lys Asp His Leu Pro Arg Leu Gly Lys Pro Ala Glu Leu Gln Arg Arg Val Ser Ala Asp Ser Gln Pro Phe Gln His Gly Asp Lys Val Lys Cys Leu Leu Asp Thr Asp Val Leu Arg Glu Met Gln Glu Gly His Gly Gly Trp Asn Pro Arg Met Ala Glu Phe Ile Gly Gln 

Thr Gly Thr Val His Arg Ile Thr Asp Arg Gly Asp Val Arg Val Gln

340 345 350

614/735

Phe	Asn	His	Glu	Thr	Arg	Trp	Thr 360	Phe	His	Pro	Gly	Ala 365	Leu	Thr	Lys
His	His 370	Ser	Phe	Trp	Val	Gly 375	Asp	Val	Val	Arg	Val 380	Ile	Gly	Asp	Leu
Asp 385	Thr	Val	Lys	Arg	Leu 390	Gln	Ala	Gly	His	Gly 395	Glu	Trp	Thr	Asp	Asp 400
Met	Ala	Pro	Ala	Leu 405	G1y	Arg	Val	Gly	Lys 410	Val	Val	Lys	Val	Phe 415	Gly
Asp	G1y	Asn	Leu 420	Arg	Val	Ala	Val	Ala 425	Gly	Gln	Arg	Trp	Thr 430	Phe	Ser
Pro	Ser	Cys 435	Leu	Val	Ala	Tyr	Arg 440	Pro	Glu	Glu	Asp	Ala 445	Asn	Leu	Asp
Val	Ala 450	Glu	Arg	Ala	Arg	G1u 455	Asn	Lys	Ser	Ser	Leu 460	Ser	Val	Ala	Leu
Asp 465	Lys	Leu	Arg	Ala	G1n 470	Lys	Ser	Asp		Glu 475	His	Pro	Gly	_	Leu 480

Arg Arg Pro Glu Gln Val Asp Thr Lys Asn Gln Gly Arg Thr Ala \$615/735\$

Val Val Glu Val Ala Leu Gly Asn Ala Ala Arg Ala Leu Asp Leu Leu

490

495

485

WO 02/0537	137			PCT/JP01/11389
	500	505	510	

Leu Gln Val Ala Ala Tyr Leu Gly Gln Val Glu Leu Ile Arg Leu Leu 515 520 525

Leu Gln Ala Arg Ala Gly Val Asp Leu Pro Asp Asp Glu Gly Asn Thr
530 535 540

Ala Leu His Tyr Ala Ala Leu Gly Asn Gln Pro Glu Ala Thr Arg Val 545 · 550 555 560

Leu Leu Ser Ala Gly Cys Arg Ala Asp Ala Ile Asn Ser Thr Gln Ser 565 570 575

Thr Ala Leu His Val Ala Val Gln Arg Gly Phe Leu Glu Val Val Arg
580 585 590

Ala Leu Cys Glu Arg Gly Cys Asp Val Asn Leu Pro Asp Ala His Ser 595 600 605

Asp Thr Pro Leu His Ser Ala Ile Ser Ala Gly Thr Gly Ala Ser Gly
610 615 620

Ile Val Glu Val Leu Thr Glu Val Pro Asn Ile Asp Val Thr Ala Thr 625 630 635 640

Asn Ser Gln Gly Phe Thr Leu Leu His His Ala Ser Leu Lys Gly His
645 650 655

Ala Leu Ala Val Arg Lys Ile Leu Ala Arg Ala Arg Gln Leu Val Asp
660 665 670

Ala Lys Lys Glu Asp Gly Phe Thr Ala Leu His Leu Ala Ala Leu Asn 675 680 685

Asn His Arg Glu Val Ala Gln Ile Leu Ile Arg Glu Gly Arg Cys Asp 690 695 700

Val Asn Val Arg Asn Arg Lys Leu Gln Ser Pro Leu His Leu Ala Val 705 710 715 720

Gln Gln Ala His Val Gly Leu Val Pro Leu Leu Val Asp Ala Gly Cys 725 730 735

Ser Val Asn Ala Glu Asp Glu Glu Gly Asp Thr Ala Leu His Val Ala 740 745 750

Leu Gln Arg His Gln Leu Leu Pro Leu Val Ala Asp Gly Ala Gly Gly
755 760 765

Asp Pro Gly Pro Leu Gln Leu Leu Ser Arg Leu Gln Ala Ser Gly Leu 770 775 780

Pro Gly Ser Ala Glu Leu Thr Val Gly Ala Ala Val Ala Cys Phe Leu 785 790 795 800

Ala Leu Glu Gly Ala Asp Val Ser Tyr Thr Asn His Arg Gly Arg Ser 805 810 815 617/735

Pro	Leu	Asp	Leu	Ala	Ala	Glu	Gly	Arg	Val	Leu	Lys	Ala	Leu	G1n	Gly
			820					825					830		
Cys	Ala	G1n 835	Arg	Phe	Arg	G1u	Arg 840	Gln	Ala	Gly	Gly	G1y 845	Ala	Ala	Pro
Gly	Pro 850	Arg	Gln	Thr	Leu	Gly 855	Thr	Pro	Asn	Thr	Val 860	Thr	Asn	Leu	His
Val 865	Gly	Ala	Ala	Pro	Gly 870	Pro	Glu	Ala	Ala	G1u 875	Cys	Leu	Val	Cys	Ser 880
G1u	Leu	Ala	Leu	Leu 885	Val	Leu	Phe	Ser	Pro 890	Cys	Gln	His	Arg	Thr 895	Val
Cys	G1u	Glu	Cys 900	Ala	Arg	Arg	Met	Lys 905	Lys	Cys	Ile	Arg	Cys 910	G1n	Val
/al	Val	Ser 915	Lys	Lys	Leu	Arg	Pro 920	Asp	G1y	Ser	Glu	Val 925	Ala	Ser	Ala
Ala	Pro 930	Ala	Pro	Gly	Pro	Pro 935	Arg	Gln	Leu	Val	Glu 940	Glu	Leu	Gln	Ser
Arg 945	Tyr	Arg	Gln	Met	G1u 950	G1u	Arg	Ile	Thr	Cys 955	Pro	Ile	Cys	Ile	Asp 960
lrg	His	Ile	Arg	Leu	Val	Phe	Gln	Cys 618/		His	Gly	Ala	Cys	Ala	Pro

965 970 975

Cys Gly Ser Ala Leu Ser Ala Cys Pro Ile Cys Arg Gln Pro Ile Arg 980 985 990

Asp Arg Ile Gln Ile Phe Val 995

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Met Gly Trp Lys Pro Ser Glu

1

5

gct aga ggc cag tcc caa agt ctc cag gca tca ggg ctg cag ccc agg 161 Ala Arg Gly Gln Ser Gln Ser Leu Gln Ala Ser Gly Leu Gln Pro Arg

10 15 20

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Ser	Leu	Lys	Ala	Ala	Arg	Arg	Ala	Thr	Gly	Arg	Pro	Asp	Arg	Ser	Arg	
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gca	gcc	ccg	ссс	aac	atg	gac	cca	gac	ccc	cag	gcg	ggc	gtg	cag	gtg	257
Ala	Ala	Pro	Pro	Asn	Met	Asp	Pro	Asp	Pro	Gln	Ala	G1y	Val	G1n	Val	
40					45					50					55	
ggc	atg	cgg	gtg	gtg	cgc	ggc	gtg	gac	tgg	aag	tgg	ggc	cag	cag	gac	305
Gly	Met	Arg	Val	Val	Arg	Gly	Val	Asp	Trp	Lys	Trp	Gly	Gln	Gln	Asp	
				60					65					70		
ggc	ggc	gag	ggc	ggc	gtg	ggc	acg	gtg	gtg	gag	ctt	ggc	cgc	cac	ggc	353
Gly	Gly	Glu	G1y	Gly	Val	Gly	Thr	Val	Val	Glu	Leu	G1y	Arg	His	Gly	
			75					80					85			
agc	ССС	tcg	aca	ccc	gac	cgc	aca	gtg	gtc	gtg	cag	tgg	gac	cag	ggc	401
Ser	Pro	Ser	Thr	Pro	Asp	Arg	Thr	Val	Val	Val	G1n	Trp	Asp	Gln	Gly	
		90					95					100				
acg	cgc	acc	aac	tac	cgc	gcc	ggc	tac	cag	ggc	gcg	cac	gac	ctg	ctg	449
Thr	Arg	Thr	Asn	Tyr	Arg	Ala	Gly	Tyr	G1n	Gly	Ala	His	Asp	Leu	Leu	
	105					110					115					
ctg	tac	gac	aac	gcc	cag	atc	ggc	gtc	cgg	cac	ссс	aac	atc	atc	tgt	497
Leu	Tyr	Asp	Asn	Ala	Gln	Ile	G1y	Val	Arg	His	Pro	Asn	Ile	Ile	Cys	
120					125					130					135	

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Asp	Cys	Cys	Lys	Lys	His	Gly	Leu	Arg	Gly	Met	Arg	Trp	Lys	Cys	Arg	
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gtg	tgc	ctg	gạc	tac	gac	ctc	tgc	acg	cag	tgc	tac	atg	cac	aac	aag	593
Val	Cys	Leu	Asp	Tyr	Asp	Leu	Cys	Thr	Gln	Cys	Tyr	Met	His	Asn	Lys	
			155					160					165			
cat	gag	ctc	gcc	cac	gcc	ttc	gac	cgc	tac	gag	acc	gct	cac	tcg	cgc	641
His	Glu	Leu	Ala	His	Ala	Phe	Asp	Arg	Tyr	Glu	Thr	Ala	His	Ser	Arg	
		170					175					180				
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cct	gtc	aca	ctg	agt	ccc	cgc	cag	ggc	ctc	ccg	agg	atc	cca	cta	agg	689
Pro	Val	Thr	Leu	Ser	Pro	Arg	G1n	Gly	Leu	Pro	Arg	Ile	Pro	Leu	Arg	
	185					190					195					
ggc	atc	ttc	cag	gga	gcg	aag	gtg	gtg	cga	ggc	ccc	ttc	tgg	gag	tgg	737
Gly	Ile	Phe	Gln	Gly	Ala	Lys	Val	Val	Arg	Gly	Pro	Phe	Trp	Glu	Trp	
200					205					210					215	
ggc	tca	cag	gat	gga	ggg	gaa	ggg	aaa	ccg	ggc	cgt	gtg	gtg	gac	atc	<b>7</b> 85
Gly	Ser	G1n	Asp	Gly	G1y	Glu	Gly	Lys	Pro	Gly	Arg	Val	Val	Asp	Ile	
				220					225					230		
cgt	ggc	tgg	gat	gtg	gag	aca	ggc	cgg	agt	gtg	gcc	agc	gtg	acg	tgg	833
Arg	Gly	Trp	Asp	Val	Glu	Thr	Gly	Arg	Ser	Val	Ala	Ser	Val	Thr	Trp	
			235					240					245			
gct	gat	ggt	acc	acc	aat	gtg	tac	cgt 621/		ggc	cac	aag	ggc	aag	gtg	881

Ala	Asp	Gly	Thr	Thr	Asn	Va1	Tyr	Arg	Val	Gly	His	Lys	Gly	Lys	Val	
		250					255					260				
gac	ctc	aag	tgt	gtg	ggc	gag	gca	gcg	ggc	ggc	ttc	tac	tac	aag	gac	929
Asp	Leu	Lys	Cys	Val	Gly	Glu	Ala	Ala	Gly	Gly	Phe	Tyr	Tyr	Lys	Asp	
	265		٠			270					275					
cac	ctc	cca	agg	ctc	ggc	aag	ccg	gcg	gag	ctg	cag	cgc	agg	gtg	agt	977
His	Leu	Pro	Arg	Leu	Gly	Lys	Pro	Ala	Glu	Leu	Gln	Arg	Arg	Val	Ser	
280					285					290					295	
gct	gac	agc	cag	ccc	ttc	cag	cac	ggg	gac	aag	gtc	aag	tgt	ctg	ctg	1025
														Leu		
	-			300					305			-	-	310		
gac	act	gat	gtc	ctg	cgg	gag	atg	cag	gaa	ggc	cac	ggc	gġc	tgg	aac	1073
														Trp		
•		-	315		_			320		·		•	325	•		
ccc	agg	atg	gcg	gag	ttt	atc	gga	cag	acg	ggc	acc	gtg	cat	cgt	atc	1121
														Arg		
		330					335					340				
acg	gac	cgc	888	gac	gtg	CEC	gte	cag	ttc	аас	cac	gag	acg	cgc	t.gg	1169
														Arg		1100
	345		<b>-</b> 2,	пор		350		0111	1110		355				115	
	040					000					000					
200	++^	000	000	aaa	aca.	cto	200			000	+00	++0	t a ~	at~	aac	1017
								_						gtg		1217
ı III.	Lue	นเร	rro	GIÀ	VIG	Դեп	ınr	Lys 622/		nıs	ser	r 116	ırp	Val	ота	

gac gtg gtc cgg gtc atc ggc gac ctt gac aca gtg aag cgg ctg cag Asp Val Val Arg Val Ile Gly Asp Leu Asp Thr Val Lys Arg Leu Gln gct ggg cat ggc gag tgg acg gac atg gcc cct gcc ctg ggc cgc Ala Gly His Gly Glu Trp Thr Asp Asp Met Ala Pro Ala Leu Gly Arg gtc ggg aag gtg gtg aaa gtg ttt gga gac ggg aac ctg cgt gta gca Val Gly Lys Val Val Lys Val Phe Gly Asp Gly Asn Leu Arg Val Ala gtc gct ggt cag cgg tgg acc ttc agc ccc tcc tgc ctg gtg gcc tac Val Ala Gly Gln Arg Trp Thr Phe Ser Pro Ser Cys Leu Val Ala Tyr cgg ccc gag gag gat gcc aac ctg gac gtg gcc gag cgc gcc cgg gag Arg Pro Glu Glu Asp Ala Asn Leu Asp Val Ala Glu Arg Ala Arg Glu aac aaa agc tca ctg agc gtg gcc ctg gac aag ctt cgg gcc cag aag Asn Lys Ser Ser Leu Ser Val Ala Leu Asp Lys Leu Arg Ala Gln Lys agt gac cca gag cac ccg gga agg ctg gtg gtg gag gtg gcg ctg ggt Ser Asp Pro Glu His Pro Gly Arg Leu Val Val Glu Val Ala Leu Gly 

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WO 02/053737

aac	gca	gcc	cgg	gct	ctg	gac	ctg	ctg	cgg	agg	cgc	cca	gag	caa	gtg	1601
Asn	Ala	Ala	Arg	Ala	Leu	Asp	Leu	Leu	Arg	Arg	Arg	Pro	Glu	Gln	Val	
		490					495					500				
gac	acc	aag	aac	caa	ggc	agg	acc	gct	ctg	caa	gtg	gct	gcc	tac	ctg	1649
Asp	Thr	Lys	Asn	G1n	Gly	Arg	Thr	Ala	Leu	Gln	Val	Ala	Ala	Tyr	Leu	
	505					510					515					
ggc	cag	gtg	gag	ttg	ata	cgg	ctg	ctg	cta	caa	gcc	agg	gcg	ggc	gtg	1697
Gly	Gln	Val	Glu	Leu	Ile	Arg	Leu	Leu	Leu	Gln	Ala	Arg	Ala	Gly	Val	
520			•		525					530					535	
gac	ctg	ccg	gac	gac	gag	ggc	aac	acg	gca	ctg	cac	tac	gcg	gcc	ctg	1745
Asp	Leu	Pro	Asp	Asp	G1u	Gly	Asn	Thr	Ala	Leu	His	Tyr	Ala	Ala	Leu	
				540					545				•	550		
ggg	aac	cag	ccc	gag	gcc	acc	agg	gtg	ctc	ctg	agt	gct	ggg	tgc	cgg	1793
Gly	Asn	Gln	Pro	Glu	Ala	Thr	Arg	Val	Leu	Leu	Ser	Ala	Gly	Cys	Arg	
			555					560					565			
gcg	gac	gcc	atc	aac	agc	acc	cag	agc	aca	gca	ctg	cac	gtg	gcc	gtg	1841
Ala	Asp	Ala	Ile	Asn	Ser	Thr	Gln	Ser	Thr	Ala	Leu	His	Val	Ala	Va1	
		570					575					580				
cag	agg	ggc	ttc	ctg	gag	gtg	gtg	cgg	gcc	ctg	tgt	gag	cgc	ggc	tgt	1889
G1n	Arg	Gly	Phe	Leu	Glu	Val	Val	Arg	Ala	Leu	Cys	Glu	Arg	Gly	Cys	
	585					590					595					

gac	gto	aac	ctg	ccc	gac	gcc	cac	tcg	gac	acg	ccc	ctg	cac	tcc	gcc	1937
Asp	Val	Asn	Leu	Pro	Asp	Ala	His	Ser	Asp	Thr	Pro	Leu	His	Ser	Ala	
600	•				605					610					615	
atc	tcg	gcg	ggc	act	gga	gcc	agc	ggc	att	gtc	gag	gtc	ctc	acg	gag	1985
Ile	Ser	Ala	G1y	Thr	Gly	Ala	Ser	Gly	Ile	Val	Glu	Val	Leu	Thr	Glu	
				620					625					630		
gtg	cca	aac	atc	gat	gtt	acc	gcc	acc	aac	agc	cag	ggt	ttc	acc	ctg	2033
Val	Pro	Asn	Ile	Asp	Val	Thr	Ala	Thr	Asn	Ser	Gln	Gly	Phe	Thr	Leu	
			635					640					645			
ctg	cac	cat	gcc	tcc	ctc	aag	ggt	cac	gcg	cta	gct	gtg	aga	aag	att	2081
Leu	His	His	Ala	Ser	Leu	Lys	Gly	His	Ala	Leu	Ala	Val	Arg	Lys	Ile	
		650					655					660				
ctg	gct	cgg	gcg	cgg	cag	ctg	gtg	gac	gcc	aag	aag	gag	gac	ggc	ttc	2129
Leu	Ala	Arg	Ala	Arg	Gln	Leu	Val	Asp	Ala	Lys	Lys	Glu	Asp	Gly	Phe	
	665					670					675					
								aac								2177
Thr	Ala	Leu	His	Leu		Ala	Leu	Asn	Asn	His	Arg	Glu	Val	Ala	G1n	
680					685					690					695	
								gac								2225
Ile	Leu	Ile	Arg		Gly	Arg	Cys	Asp		Asn	Val	Arg	Asn	Arg	Lys	
				700					705					710		
ctg	cag	tcc	ccg	ctg	cat	ctc	gcc	gtg 625/		cag	gcc	cac	gtg	ggg	ctg	2273

Leu Gln Ser Pro Leu His Leu Ala Val Gln Gln Ala His Val Gly Leu gtg ccg cta ctg gtg gac gct ggg tgc agt gtc aac gcc gag gac gag Val Pro Leu Leu Val Asp Ala Gly Cys Ser Val Asn Ala Glu Asp Glu gag ggg gac aca gcc ctg cac gtg gcg ctg cag cgt cat cag ctg ctg Glu Gly Asp Thr Ala Leu His Val Ala Leu Gln Arg His Gln Leu Leu ccc ctg gtg gct gat ggg gcc ggg ggg gac cca ggg ccc ttg cag ctg Pro Leu Val Ala Asp Gly Ala Gly Gly Asp Pro Gly Pro Leu Gln Leu ctg tcc agg cta cag gcc tcg ggc ctc ccc ggc agc gcg gag ctg acg Leu Ser Arg Leu Gln Ala Ser Gly Leu Pro Gly Ser Ala Glu Leu Thr gtg ggc gcg gcg gtc gcc tgc ttc ctg gcg ctg gag ggc gcc gac gtg Val Gly Ala Ala Val Ala Cys Phe Leu Ala Leu Glu Gly Ala Asp Val age tac ace aac cac ege ggt egg age eeg etg gae etg gee gee gag Ser Tyr Thr Asn His Arg Gly Arg Ser Pro Leu Asp Leu Ala Ala Glu 

ggt cgc gtg ctc aag gcc ctt cag ggc tgc gcc cag cgc ttc cgg gag

Gly Arg Val Leu Lys Ala Leu Gln Gly Cys Ala Gln Arg Phe Arg Glu

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825 830 835

cgg cag gcg ggc ggg ggc gcg gcc ccg ggc ccc agg caa acg ctc ggg 2657

Arg Gln Ala Gly Gly Gly Ala Ala Pro Gly Pro Arg Gln Thr Leu Gly

840 845 850 855

acc ccc aac acc gtg acg aac ctg cac gtg ggc gcc gcg ccg ggg ccc 2705

Thr Pro Asn Thr Val Thr Asn Leu His Val Gly Ala Ala Pro Gly Pro

860 865 870

gag gcc gct gag tgc ctg gtg tgc tcc gag ctg gcg ctg ctg gtg ctg 2753
Glu Ala Ala Glu Cys Leu Val Cys Ser Glu Leu Ala Leu Leu Val Leu
875
880
885

ttc tcg ccg tgc cag cac cgc acc gtg tgt gag gag tgc gcg cgc agg 2801
Phe Ser Pro Cys Gln His Arg Thr Val Cys Glu Glu Cys Ala Arg Arg
890 895 . 900

atg aag aag tgc atc agg tgc cag gtg gtc gtc agc aag aaa ctg cgc 2849

Met Lys Lys Cys Ile Arg Cys Gln Val Val Val Ser Lys Lys Leu Arg

905 910 915

cca gac ggc tct gag gtg gcg agc gcc ccc gcc ccc ggc ccg ccg 2897

Pro Asp Gly Ser Glu Val Ala Ser Ala Ala Pro Ala Pro Gly Pro Pro

920 925 930 935

cgc cag ctg gtg gag gag ctg cag agc cgc tac cgg cag atg gag gaa 2945 Arg Gln Leu Val Glu Glu Leu Gln Ser Arg Tyr Arg Gln Met Glu Glu 940 945 950

cgc atc acc tgc ccc atc tgc atc gac agc cac atc cgc ctc gtg ttc 2993

Arg Ile Thr Cys Pro Ile Cys Ile Asp Ser His Ile Arg Leu Val Phe
955 960 965

cag tgc ggc cac ggc gca tgc gcc ccc tgc ggc tcc gcg ctc agc gcc 3041

Gln Cys Gly His Gly Ala Cys Ala Pro Cys Gly Ser Ala Leu Ser Ala

970 975 980

tgc ccc atc tgc cgc cag ccc atc cgc gac cgc atc cag atc ttc gtg 3089

Cys Pro Ile Cys Arg Gln Pro Ile Arg Asp Arg Ile Gln Ile Phe Val

985 990 995

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aaaagaaaga ttctcggat 3168

<210> 162

<211> 999

<212> PRT

<213> Homo sapiens

<400> 162

Met Gly Trp Lys Pro Ser Glu Ala Arg Gly Gln Ser Gln Ser Leu Gln

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Ala Ser Gly Leu Gln Pro Arg Ser Leu Lys Ala Ala Arg Arg Ala Thr
20 25 30

Gly	Arg	Pro	Asp	Arg	Ser	Arg	Ala	Ala	Pro	Pro	Asn	Met	Asp	Pro	Asp
		35					40					45			
Pro	Gln	Ala	Gly	Val	Gln	Val	Gly	Met	Arg	Val	Va1	Arg	Gly	Val	Asp
	50					55					60				
Trp	Lys	Trp	Gly	Gln	Gln	Asp	Gly	Gly	G1u	Gly	Gly	Val	Gly	Thr	Val
65					70					75					80
Val	Glu	Leu	Gly	Arg	His	G1y	Ser	Pro	Ser	Thr	Pro	Asp	Arg	Thr	Val
				85					90					95	
Val	Val	Gln	Trp	Asp	Gln	Gly	Thr	Arg	Thr	Asn	Tyr	Arg	Ala	Gly	Tyr
			100					105					110		
G1n	Gly	Ala	His	Asp	Leu	Leu	Leu	Tyr	Asp	Asn	Ala	Gln	Ile	Gly	Val
		115					120					125			
Arg	His	Pro	Asn	Ile	Ile	Cys	Asp	Cys	Cys	Lys	Lys	His	Gly	Leu	Arg
	130					135					140				
Gly	Met	Arg	Trp	Lys	Cys	Arg	Val	Cys	Leu	Asp	Tyr	Asp	Leu	Cys	Thr
145					150					155					160
Gln	Cys	Tyr	Met	His	Asn	Lys	His	Glu	Leu	Ala	His	Ala	Phe	Asp	Arg
	-	-	-	165		-			170					175	- 3

Tyr Glu Thr Ala His Ser Arg Pro Val Thr Leu Ser Pro Arg Gln Gly

180 185 190

Leu Pro Arg Ile Pro Leu Arg Gly Ile Phe Gln Gly Ala Lys Val Val 195 200 205

Arg Gly Pro Phe Trp Glu Trp Gly Ser Gln Asp Gly Gly Glu Gly Lys
210 215 220

Pro Gly Arg Val Val Asp Ile Arg Gly Trp Asp Val Glu Thr Gly Arg 225 230 235 240

Ser Val Ala Ser Val Thr Trp Ala Asp Gly Thr Thr Asn Val Tyr Arg
245 250 255

Val Gly His Lys Gly Lys Val Asp Leu Lys Cys Val Gly Glu Ala Ala 260 265 270

Gly Gly Phe Tyr Tyr Lys Asp His Leu Pro Arg Leu Gly Lys Pro Ala 275 280 285

Glu Leu Gln Arg Arg Val Ser Ala Asp Ser Gln Pro Phe Gln His Gly
290 295 300

Asp Lys Val Lys Cys Leu Leu Asp Thr Asp Val Leu Arg Glu Met Gln 305 310 315 320

Glu Gly His Gly Gly Trp Asn Pro Arg Met Ala Glu Phe Ile Gly Gln 325 330 335

Thr	Gly	Thr	Val	His	Arg	Ile	Thr	Asp	Arg	Gly	Asp	Val	Arg	Val	G1n
			340					345					350		

Phe Asn His Glu Thr Arg Trp Thr Phe His Pro Gly Ala Leu Thr Lys
355 360 365

His His Ser Phe Trp Val Gly Asp Val Val Arg Val Ile Gly Asp Leu 370 375 380

Asp Thr Val Lys Arg Leu Gln Ala Gly His Gly Glu Trp Thr Asp Asp 385 390 395 400

Met Ala Pro Ala Leu Gly Arg Val Gly Lys Val Val Lys Val Phe Gly
405 410 415

Asp Gly Asn Leu Arg Val Ala Val Ala Gly Gln Arg Trp Thr Phe Ser 420 425 430

Pro Ser Cys Leu Val Ala Tyr Arg Pro Glu Glu Asp Ala Asn Leu Asp
435
440
445

Val Ala Glu Arg Ala Arg Glu Asn Lys Ser Ser Leu Ser Val Ala Leu
450 455 460

Asp Lys Leu Arg Ala Gln Lys Ser Asp Pro Glu His Pro Gly Arg Leu 465 470 475 480

Val Val Glu Val Ala Leu Gly Asn Ala Ala Arg Ala Leu Asp Leu Leu
485 490 495
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Arg	Arg	Arg	Pro 500	Glu	Gln	Val	Asp	Thr 505	Lys	Asn	Gln	Gly	Arg 510	Thr	Ala
Leu	Gln	Val 515	Ala	Ala	Tyr	Leu	Gly 520	Gln	Val	Glu	Leu	Ile 525	Arg	Leu	Leu
Leu	G1n 530	Ala	Arg	Ala	Gly	Val 535	Asp	Leu	Pro	Asp	Asp 540	G1u	Gly	Asn	Thr
Ala 545	Leu	His	Tyr	Ala	Ala 550	Leu	Gly	Asn	G1n	Pro 555	Glu	Ala	Thr	Arg	Val 560
Leu	Leu	Ser	Ala	Gly 565	Cys	Arg	Ala	Asp	Ala 570	Ile	Asn	Ser	Thr	G1n 575	Ser
Thr	Ala	Leu	His 580	Val	Ala	Val	Gln	Arg 585	Gly	Phe	Leu	Glu	Val 590	Val	Arg
Ala	Leu	Cys 595	Glu	Arg	Gly	Cys	Asp 600	Val	Asn	Leu	Pro	Asp 605	Ala	His	Ser
Asp	Thr 610	Pro	Leu	His	Ser	Ala 615	Ile	Ser	Ala	Gly	Thr 620	Gly	Ala	Ser	Gly
Ile 625	Val	G1u	Val	Leu	Thr 630	Glu	Val	Pro	Asn	Ile 635	Asp	Val	Thr		Thr 640

Asn Ser Gln Gly Phe Thr Leu Leu His His Ala Ser Leu Lys Gly His

645 650 655

Ala Leu Ala Val Arg Lys Ile Leu Ala Arg Ala Arg Gln Leu Val Asp
660 665 670

Ala Lys Lys Glu Asp Gly Phe Thr Ala Leu His Leu Ala Ala Leu Asn 675 680 685

Asn His Arg Glu Val Ala Gln Ile Leu Ile Arg Glu Gly Arg Cys Asp 690 695 700

Val Asn Val Arg Asn Arg Lys Leu Gln Ser Pro Leu His Leu Ala Val 705 710 715 720

Gln Gln Ala His Val Gly Leu Val Pro Leu Leu Val Asp Ala Gly Cys
725 730 735

Ser Val Asn Ala Glu Asp Glu Glu Gly Asp Thr Ala Leu His Val Ala 740 745 750

Leu Gln Arg His Gln Leu Leu Pro Leu Val Ala Asp Gly Ala Gly Gly
755 760 765

Asp Pro Gly Pro Leu Gln Leu Leu Ser Arg Leu Gln Ala Ser Gly Leu
770 775 780

Pro Gly Ser Ala Glu Leu Thr Val Gly Ala Ala Val Ala Cys Phe Leu 785 790 795 800

Ala	Leu	Glu	Gly	Ala 805	Asp	Val	Ser	Tyr	Thr 810	Asn	His	Arg	Gly	Arg 815	Ser
Pro	Leu	Asp	Leu 820	Ala	Ala	Glu	Gly	Arg 825	Val	Leu	Lys	Ala	Leu 830	G1n	Gly
Cys	Ala	G1n 835	Arg	Phe	Arg	Glu	Arg 840	Gln	Ala	Gly	Gly	Gly 845	Ala	Ala	Pro
Gly	Pro 850	Arg	Gln	Thr	Leu	Gly 855	Thr	Pro	Asn	Thr	Val 860	Thr	Asn	Leu	His
Val 865	Gly	Ala	Ala	Pro	Gly 870	Pro	Glu	Ala	Ala	Glu 875	Cys	Leu	Val	Cys	Ser 880
Glu	Leu	Ala	Leu	Leu 885	Val	Leu	Phe	Ser	Pro 890	Cys	G1n	His	Arg	Thr 895	Val
Cys	Glu	Glu	Cys 900	Ala	Arg	Arg	Met	Lys 905	Lys	Cys	Ile	Arg	Cys 910	Gln	Val
Val	Val	Ser 915	Lys	Lys	Leu	Arg	Pro 920	Asp	Gly	Ser	Glu	Val 925	Ala	Ser	Ala
Ala	Pro 930	Ala	Pro	Gly	Pro	Pro 935	Arg	Gln	Leu	Val	G1u 940	Glu	Leu	Gln	Ser

Arg Tyr Arg Gln Met Glu Glu Arg Ile Thr Cys Pro Ile Cys Ile Asp

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950

955

960

945

Ser His Ile Arg Leu Val Phe Gln Cys Gly His Gly Ala Cys Ala Pro 965 970 975

Cys Gly Ser Ala Leu Ser Ala Cys Pro Ile Cys Arg Gln Pro Ile Arg 980 985 990

Asp Arg Ile Gln Ile Phe Val 995

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Met Ile Ala Trp Arg Leu Pro Leu

1

5

tgc gtg ctc ttg gtg gcc tcc gtc gag agc cac ctg ggg gcc ctg ggg 162 635/735

Cys	Val	Leu	Leu	Val	Ala	Ser	Val	Glu	Ser	His	Leu	Gly	Ala	Leu	G1y	
	10					15					20					
															gcg	210
	Lys	Asn	Val	Ser		Lys	Asp	Ala	Glu			Arg	Thr	Tyr		
25					30					35					40	
gac	gac	gtc	aac	age	gag	ctø	øtc	aac	atc	tac	acc	ttc	220	cac	200	258
								Asn								200
изр	пор	101	11311	45	Olu	Leu	191	nsn	50	1 9 1	1111	1 He	ASII	55	1111	
				10					50					55		
gtg	acc	cgc	aac	cgg	acc	gag	ggt	gtg	cga	gtg	tct	gtg	aat	gtc	ctg	306
								Val								
			60					65					70			
aac	aag	cag	aaa	ggg	gcg	cct	ttg	ctg	ttc	gtg	gtc	cgc	cag	aag	gag	354
Asn	Lys	G1n	Lys	Gly	Ala	Pro	Leu	Leu	Phe	Val	Val	Arg	Gln	Lys	Glu	
		75					80					85				
gct	gtt	gtg	tcc	ttc	cag	gtg	ccc	cta	atc	ctt	cga	gga	ctg	tat	cag	402
Ala	Val	Val	Ser	Phe	Gln	Val	Pro	Leu	Ile	Leu	Arg	Gly	Leu	Tyr	Gln	
	90					95					100					
	`															
cgg	aag	tac	ctc	tac	caa	aaa	gtg	gaa	cga	act	ctg	tgt	cag	ccc	ccc	450
Arg	Lys	Tyr	Leu	Tyr	G1n	Lys	Val	Glu	Arg	Thr	Leu	Cys	G1n	Pro	Pro	
105					110					115					120	
								ttt								498
ſhr	Lys	Asn	Glu	Ser	G1u	Ile	Gln	Phe 636/		Tyr	Val	Asp	Val	Ser	Thr	
								000/	, ,,,							

125 130 135

ctg tca ccc gtc aat acc act tac cag ctc cga gtc aac cgt gtg gac 546

Leu Ser Pro Val Asn Thr Thr Tyr Gln Leu Arg Val Asn Arg Val Asp

140 145 150

aat ttt gtg ctc agg act gga gag ctg ttt acc ttt aat acc act gca 594
Asn Phe Val Leu Arg Thr Gly Glu Leu Phe Thr Phe Asn Thr Thr Ala
155 160 165

gcc cag ccc cag tac ttc aaa tac gag ttt cct gat ggt gtg gac tcg 642
Ala Gln Pro Gln Tyr Phe Lys Tyr Glu Phe Pro Asp Gly Val Asp Ser
170 175 180

gta att gtc aag gtg acc tcc aag aag gcc ttc ccc tgc tca gtc atc 690
Val Ile Val Lys Val Thr Ser Lys Lys Ala Phe Pro Cys Ser Val Ile
185 190 195 200

tcc atc cag gat gtc ctg tgc cct gtc tat gat ctg gac aac agt gta 738

Ser Ile Gln Asp Val Leu Cys Pro Val Tyr Asp Leu Asp Asn Ser Val

205 210 215

gcc ttc att ggc atg tac cag acg atg act aag aag gca gcc atc act 786

Ala Phe Ile Gly Met Tyr Gln Thr Met Thr Lys Lys Ala Ala Ile Thr

220 225 230

gtg cag cgg aaa gac ttc ccc agc aac agc ttc tat gtg gtg gtg gta 834 Val Gln Arg Lys Asp Phe Pro Ser Asn Ser Phe Tyr Val Val Val Val 235 240 245

gtg	aag	act	gag	gac	cag	gcc	tgc	gga	ggg	tcc	ttg	ccc	ttc	tac	cct	882
Val	Lys	Thr	Glu	Asp	Gln	Ala	Cys	Gly	Gly	Ser	Leu	Pro	Phe	Tyr	Pro	
	250					255					260					
ttt	gtg	gaa	gat	gag	cca	gtg	gat	caa	ggg	cac	cgt	cag	aaa	aca	ctg	930
Phe	Val	Glu	Asp	Glu	Pro	Val	Asp	Gln	Gly	His	Arg	Gln	Lys	Thr	Leu	
265					270					275					280	
tca	gtg	ctg	gtc	tct	cag	gct	gtc	aca	tct	gag	gcc	tat	gtt	ggt	ggg	978
Ser	Val	Leu	Val	Ser	Gln	Ala	Val	Thr	Ser	Glu	Ala	Tyr	Val	Gly	Gly	
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atg	ctc	ttt	tgc	ctg	ggc	ata	ttc	ttg	tcc	ttc	tac	ctg	ctg	act	gtg	1026
Met	Leu	Phe	Cys	Leu	Gly	Ile	Phe	Leu	Ser	Phe	Tyr	Leu	Leu	Thr	Val	
			300		-			305					310			
											•					
ctg	ctg	gcc	tgt	tgg	gag	aac	tgg	agg	caa	agg	aag	aag	acc	ttg	ctg	1074
Leu	Leu	Ala	Cys	Trp	Glu	Asn	Trp	Arg	Gln	Arg	Lys	Lys	Thr	Leu	Leu	
		315					320					325				
gtg	gcc	ata	gac	cga	gcc	tgc	cca	gaa	agt	ggt	cac	gct	cgg	gtc	ttg	1122
Val	Ala	Ile	Asp	Arg	Ala	Cys	Pro	G1u	Ser	Gly	His	Ala	Arg	Val	Leu	
	330					335					340					
gct	gat	tca	ttt	cct	ggc	agt	gcc	cct	tac	gag	ggt	tac	aac	tat	ggc	1170
Ala	Asp	Ser	Phe	Pro	Gly	Ser	Ala	Pro	Tyr	G1u	Gly	Tyr	Asn	Tyr	Gly	
345					350					355					360	

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S	Ser	Phe	Glu	Asn	Gly	Ser	Gly	Ser	Thr	Asp	Gly	Leu	Val	Glu	Ser	Ala	
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8	gt	tca	ggg	gac	ctc	tcc	tac	agt	tac	cag	ggg	cac	gac	cag	ttc	aag	1266
G	lу	Ser	Gly	Asp	Leu	Ser	Tyr	Ser	Tyr	Gln	Gly	His	Asp	Gln	Phe	Lys	
				380					385					390			
c	gg	cgc	ctt	ссс	tct	ggc	cag	atg	cgg	cag	ctg	tgc	att	gcc	atg	gac	1314
A	rg	Arg	Leu	Pro	Ser	Gly	G1n	Met	Arg	Gln	Leu	Cys	Ile	Ala	Met	Asp	
			395					400					405				
С	gc	tcc	ttt	gac	gca	gtg	ggt	cct	cgg	cct	cga	ctg	gac	tcc	atg	agc	1362
A	rg	Ser	Phe	Asp	Ala	Val	Gly	Pro	Arg	Pro	Arg	Leu	Asp	Ser	Met	Ser	
		410					415					420					
t	СС	gtg	gaa	gag	gat	gac	tac	gac	acg	ctg	act	gac	atc	gac	tca	gac	1410
S	er	Val	Glu	Glu	Asp	Asp	Tyr	Asp	Thr	Leu	Thr	Asp	Ile	Asp	Ser	Asp	
4	25					430					435					440	
a	aa	aac	gtc	att	cga	acc	aag	caa	tac	ctc	tgt	gtg	gct	gat	ctg	gca	1458
L	ys	Asn	Val	Ile	Arg	Thr	Lys	Gln	Tyr	Leu	Cys	Val	Ala	Asp	Leu	Ala	
					445					450					455		
Cį	ga	aag	gac	aaa	cgt	gtt	ttg	cgg	aaa	aag	tac	cag	att	tac	ttc	tgg	1506
A	rg	Lys	Asp	Lys	Arg	Val	Leu	Arg	Lys	Lys	Tyr	G1n	Ile	Tyr	Phe	Trp	•
				460					465					470			
	٠																
aa	ac	ata	gcc	acc	att	gcg	gtc	ttc	tac 639/		ctt	cct	gtg	gtg	cag	ctg	1554

Asn Ile Ala Thr Ile Ala Val Phe Tyr Ala Leu Pro Val Val Gln Leu
475 480 485

gtg atc acc tac cag acg gtg gtg aat gtc aca ggg aac cag gac atc 1602

Val Ile Thr Tyr Gln Thr Val Val Asn Val Thr Gly Asn Gln Asp Ile

490 495 500

tgc tac tac aac ttc ctc tgt gcc cac ccg ctg ggc aac ctc agc gcc 1650 Cys Tyr Tyr Asn Phe Leu Cys Ala His Pro Leu Gly Asn Leu Ser Ala 505 510 515 520

ttc aac aac atc ctc agc aac ttg ggg tac atc ctg ctg ggg ctg ctc 1698

Phe Asn Asn Ile Leu Ser Asn Leu Gly Tyr Ile Leu Leu Gly Leu Leu

525 530 535

ttc ctg ctc atc atc ctg cag cga gag atc aat cat aac cgg gcc ctg 1746

Phe Leu Leu Ile Ile Leu Gln Arg Glu Ile Asn His Asn Arg Ala Leu
540 545 550

ctg cgg aat gac ctc tat gct ctg gag tgt ggg atc ccc aaa cac ttt 1794 Leu Arg Asn Asp Leu Tyr Ala Leu Glu Cys Gly Ile Pro Lys His Phe 555 560 565

ggt ctg ttt tac gcc atg ggc aca gca ctg atg gag ggg cta ctt 1842 Gly Leu Phe Tyr Ala Met Gly Thr Ala Leu Met Met Glu Gly Leu Leu 570 575 580

agt gcc tgt tac cac gtc tgc ccc aac tac acc aac ttc cag ttt gat 1890 Ser Ala Cys Tyr His Val Cys Pro Asn Tyr Thr Asn Phe Gln Phe Asp 640/735

585					590					595					600	
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Thr	Ser	Phe	Met	Tyr	Met	Ile	Ala	Gly	Leu	Cys	Met	Leu	Lys	Leu	Tyr	
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cag	aag	cgg	cac	cca	gat	atc	aac	gcc	agt	gcc	tac	agt	gca	tat	gcc	1986
Gln	Lys	Arg	His	Pro	Asp	Ile	Asn	Ala	Ser	Ala	Tyr	Ser	Ala	Tyr	Ala	
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tgc	ttg	gcc	atc	gtc	atc	ttc	ttc	tcc	gtt	ctg	ggc	gtg	gtg	ttt	ggc	2034
Cys	Leu	Ala	Ile	Val	Ile	Phe	Phe	Ser	Val	Leu	Gly	Val	Val	Phe	Gly	
		635					640					645				
aaa	ggg	aac	acg	gcc	ttc	tgg	att	gtc	ttc	tcc	gtc	att	cac	atc	atc	2082
Lys	Gly	Asn	Thr	Ala	Phe	Trp	Ile	Val	Phe	Ser	Val	Ile	His	Ile	Ile	
	650					655					660					
tcc	acc	ctg	ctc	ctc	agc	act	cag	ctc	tat	tac	atg	ggc	cgc	tgg	aag	2130
Ser	Thr	Leu	Leu	Leu	Ser	Thr	Gln	Leu	Tyr	Tyr	Met	Gly	Arg	Trp	Lys	
665					670					675					680	
ctg	gac	ttc	ggg	atc	ttc	cgc	cgc	atc	ctc	cat	gtg	ctc	tac	aca	gac	2178
Leu	Asp	Phe	Gly	Ile	Phe	Arg	Arg	Ile	Leu	His	Val	Leu	Tyr	Thr	Asp	
				685					690					695	-	
tgc	atc	cgg	cag	tgc	agc	ggg	ccc	ctt	tac	acg	gac	cgc	atg	gtg	ctt	2226
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-		Ū	700	•		•		705	•		•	-	710		<del>-</del>	

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PCT/JP01/11389

WO 02/053737

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Le	u Val	. Met	G1y	Asn	Ile	Ile	Asn	Trp	Ser	Leu	Ala	Ala	Tyr	Gly	Leu	•
		715					720					725				
ato	ate	cgc	ccc	aat	gac	ttt	gct	tcc	tac	ttg	ctg	gca	att	ggc	atc	2322
110	e Met	Arg	Pro	Asn	Asp	Phe	Ala	Ser	Tyr	Leu	Leu	Ala	Ile	Gly	Ile	
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tgo	aac	ctg	ctg	ctt	tat	ttc	gcc	ttc	tac	atc	atc	atg	aag	ctc	cgg	2370
Cys	s Asn	Leu	Leu	Leu	Tyr	Phe	Ala	Phe	Tyr	Ile	Ile	Met	Lys	Leu	Arg	
745	5				750					755					760	
ago	ggc	gag	agg	atc	aag	ctc	atc	cct	ctg	ctt	tgc	atc	gtc	tgc	acc	2418
Ser	· Gly	G1u	Arg	Ile	Lys	Leu	Ile	Pro	Leu	Leu	Cys	Ile	Val	Cys	Thr	
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Ser	Val	Val	Trp	Gly	Phe	Ala	Leu	Phe	Phe	Phe	Phe	G1n	Gly	Leu	Ser	
	•		780					785					790			
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Thr	Trp	Gln	Lys	Thr	Pro	Ala	Glu	Ser	Arg	Glu	His	Asn	Arg	Asp	Cys	
		795					800					805				
atc	ctc	ctc	gac	ttc	ttt	gat	gac	cac	gat	atc	tgg	cac	ttc	ctg	tcc	2562
Ile	Leu	Leu	Asp	Phe	Phe	Asp	Asp	His	Asp	Ile	Trp	His	Phe	Leu	Ser	
	810					815					820					

tcc att gcc atg ttt ggg tcc ttc ctg gtt ttg ctg acg ttg gat gac 2610

Ser Ile Ala Met Phe Gly Ser Phe Leu Val Leu Leu Thr Leu Asp Asp

825 830 835 840

gac ttg gac aca gta cag cgg gac aag atc tat gtc ttc tagcagcatc 2659
Asp Leu Asp Thr Val Gln Arg Asp Lys Ile Tyr Val Phe
845 850

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Ala Glu Phe Glu Arg Thr Tyr Ala Asp Asp Val Asn Ser Glu Leu Val
35 40 45

Asn Ile Tyr Thr Phe Asn His Thr Val Thr Arg Asn Arg Thr Glu Gly
50 55 60

Val Arg Val Ser Val Asn Val Leu Asn Lys Gln Lys Gly Ala Pro Leu 65 70 75 80

Leu Phe Val Val Arg Gln Lys Glu Ala Val Val Ser Phe Gln Val Pro 85 90 95

Leu Ile Leu Arg Gly Leu Tyr Gln Arg Lys Tyr Leu Tyr Gln Lys Val 100 105 110

Glu Arg Thr Leu Cys Gln Pro Pro Thr Lys Asn Glu Ser Glu Ile Gln 115 120 125

Phe Phe Tyr Val Asp Val Ser Thr Leu Ser Pro Val Asn Thr Tyr

130 135 140
645/735

Gln	Leu	Arg	Val	Asn	Arg	Val	Asp	Asn	Phe	Val	Leu	Arg	Thr	Gly	G1u
145					150					155					160
Leu	Phe	Thr	Phe	Asn 165	Thr	Thr	Ala	Ala	Gln 170	Pro	G1n	Tyr	Phe	Lys 175	
Glu	Phe	Pro	Asp 180	Gly	Val	Asp	Ser	Val 185	Ile	Val	Lys	Val	Thr 190	Ser	Lys
Lys	Ala	Phe 195	Pro	Cys	Ser	Val	Ile 200	Ser	Ile	G1n	Asp	Val 205	Leu	Cys	Pro
Val	Tyr 210	Asp	Leu	Asp	Asn	Ser 215	Val	Ala	Phe	Ile	Gly 220	Met	Tyr	Gln	Thr
Met 225	Thr	Lys	Lys	Ala	Ala 230	Ile	Thr	Val	G1n	Arg 235	Lys	Asp	Phe	Pro	Ser 240
Asn	Ser	Phe	Tyr	Val 245	Val	Val	Val	Val	Lys 250	Thr	Glu	Asp	Gln	Ala 255	Cys
Gly	Gly	Ser	Leu 260	Pro	Phe	Tyr	Pro	Phe 265	Val	Glu	Asp	Glu	Pro 270	Val	Asp
Gln	Gly	His 275	Arg	Gln	Lys	Thr	Leu 280	Ser	Val	Leu	Val	Ser 285	G1n	Ala	Val
Thr	Ser	Glu	Ala	Tyr	Val	Gly	Gly	Met	Leu	Phe	Cys	Leu	Gly	Ile	Phe

290 295 300

Leu Ser Phe Tyr Leu Leu Thr Val Leu Leu Ala Cys Trp Glu Asn Trp 305 310 315 320

Arg Gln Arg Lys Lys Thr Leu Leu Val Ala Ile Asp Arg Ala Cys Pro 325 330 335

Glu Ser Gly His Ala Arg Val Leu Ala Asp Ser Phe Pro Gly Ser Ala : 340 345 350

Pro Tyr Glu Gly Tyr Asn Tyr Gly Ser Phe Glu Asn Gly Ser Gly Ser 355 360 365

Thr Asp Gly Leu Val Glu Ser Ala Gly Ser Gly Asp Leu Ser Tyr Ser 370 375 380

Tyr Gln Gly His Asp Gln Phe Lys Arg Arg Leu Pro Ser Gly Gln Met 385 390 395 400

Arg Gln Leu Cys Ile Ala Met Asp Arg Ser Phe Asp Ala Val Gly Pro 405 410 415

Arg Pro Arg Leu Asp Ser Met Ser Ser Val Glu Glu Asp Asp Tyr Asp
420
425
430

Thr Leu Thr Asp Ile Asp Ser Asp Lys Asn Val Ile Arg Thr Lys Gln
435
440
445

Tyr	Leu 450	Cys	Val	Ala	Asp	Leu 455	Ala	Arg	Lys	Asp	Lys 460	Arg	Val	Leu	Arg
Lys 465	Lys	Tyr	Gln	Ile	Tyr 470	Phe	Trp	Asn	Ile	Ala 475	Thr	Ile	Ala	Val	Phe 480
Tyr	Ala	Leu	Pro	Val 485	Val	G1n	Leu	Val	Ile 490	Thr	Tyr	Gln	Thr	Val 495	Val
Asn	Val	Thr	Gly 500	Asn	G1n	Asp	Ile	Cys 505	Tyr	Tyr	Asn	Phe	Leu 510	Cys	Ala
His	Pro	Leu 515	Gly	Asn	Leu	Ser	Ala 520	Phe	Asn	Asn	Ile	Leu 525	Ser	Asn	Leu
Gly	Tyr 530	Ile	Leu	Leu	Gly	Leu 535	Leu	Phe	Leu	Leu	Ile 540	Ile	Leu	Gln	Arg
Glu 545	Ile	Asn	His	Asn	Arg 550	Ala	Leu	Leu	Arg	Asn 555	Asp	Leu	Tyr	Ala	Leu 560
G1u	Cys	Gly	Ile	Pro 565	Lys	His	Phe	Gly	Leu 570	Phe	Tyr	Ala	Met	Gly 575	Thr

Asn Tyr Thr Asn Phe Gln Phe Asp Thr Ser Phe Met Tyr Met Ile Ala
595 600 605
648/735

Ala Leu Met Met Glu Gly Leu Leu Ser Ala Cys Tyr His Val Cys Pro

585

590

580

Gly	Leu	Cys	Met	Leu	Lys	Leu	Tyr	Gln	Lys	Arg	His	Pro	Asp	Ile	Ası
	610					615					620				
Ala 625	Ser	Ala	Tyr	Ser	Ala 630	Tyr	Ala	Cys	Leu	Ala 635	Ile	Val	Ile	Phe	Phe 640
Ser	Val	Leu	Gly	Val 645	Val	Phe	Gly	Lys	Gly 650	Asn	Thr	Ala	Phe	Trp 655	Ιlϵ
Val	Phe	Ser	Val 660	Ile	His	Ile	Ile	Ser 665	Thr	Leu	Leu	Leu	Ser 670	Thr	G1r
Leu	Tyr	Tyr 675	Met	Gly	Arg	Trp	Lys 680	Leu	Asp	Phe	Gly	Ile 685	Phe	Arg	Arg
Ile	Leu 690	His	Val	Leu	Tyr	Thr 695	Asp	Cys	Ile	Arg	Gln 700	Cys	Ser	Gly	Pro
Leu 705	Tyr	Thr	Asp	Arg	Met 710	Val	Leu	Leu	Val	Met 715	Gly	Asn	Ile	Ile	Asr.
Trp	Ser	Leu	Ala	Ala 725	Tyr	Gly	Leu	Ile	Met 730	Arg	Pro	Asn	Asp	Phe 735	Ala
Ser	Tyr	Leu	Leu	Ala	Ile	Gly	Ile	Cys	Asn	Leu	Leu	Leu	Tyr	Phe	Ala

Phe Tyr Ile Ile Met Lys Leu Arg Ser Gly Glu Arg Ile Lys Leu Ile \$649/735\$

745

740

750

755 760 765

Pro Leu Cys Ile Val Cys Thr Ser Val Val Trp Gly Phe Ala Leu 770 775 780

Phe Phe Phe Phe Gln Gly Leu Ser Thr Trp Gln Lys Thr Pro Ala Glu
785 790 795 800

Ser Arg Glu His Asn Arg Asp Cys IIe Leu Leu Asp Phe Phe Asp Asp 805 810 815

His Asp Ile Trp His Phe Leu Ser Ser Ile Ala Met Phe Gly Ser Phe 820 825 830

Leu Val Leu Leu Thr Leu Asp Asp Leu Asp Thr Val Gln Arg Asp 835 840 845

Lys Ile Tyr Val Phe 850

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Met Phe Ala Leu Gly Leu Pro Phe Leu Val

1

5 10

ctc ttg gtg gcc tcg gtc gag agc cat ctg ggg gtt ctg ggg ccc aag 161 Leu Leu Val Ala Ser Val Glu Ser His Leu Gly Val Leu Gly Pro Lys 15 20 25

aac gtc tcg cag aaa gac gcc gag ttt gag cgc acc tac gtg gac gag 209
Asn Val Ser Gln Lys Asp Ala Glu Phe Glu Arg Thr Tyr Val Asp Glu
30 35 40

gtc aac agc gag ctg gtc aac atc tac acc ttc aac cat act gtg acc 257

Val Asn Ser Glu Leu Val Asn Ile Tyr Thr Phe Asn His Thr Val Thr

45 50 55

cgc aac agg aca gag ggc gtg cgt gtg tct gtg aac gtc ctg aac aag 305 Arg Asn Arg Thr Glu Gly Val Arg Val Ser Val Asn Val Leu Asn Lýs 60 65 70

cag aag ggg gcg ccg ttg ctg ttt gtg gtc cgc cag aag gag gct gtg 353
Gln Lys Gly Ala Pro Leu Leu Phe Val Val Arg Gln Lys Glu Ala Val
75 80 85 90

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Val	Ser	Phe	Gln	Val	Pro	Leu	Ile	Leu	Arg	Gly	Met	Phe	Gln	Arg	Lys	
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tac	ctc	tac	caa	aaa	gtg	gaa	cga	acc	ctg	tgt	cag	ccc	ccc	acc	aag	449
Tyr	Leu	Tyr	Gln	Lys	Val	Glu	Arg	Thr	Leu	Cys	Gln	Pro	Pro	Thr	Lys	
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aat	gag	tcg	gag	att	cag	ttc	ttc	tac	gtg	gat	gtg	tcc	acc	ctg	tca	497
Asn	Glu	Ser	Glu	Ile	Gln	Phe	Phe	Tyr	Val	Asp	Val	Ser	Thr	Leu	Ser	
		125					130					135				
cca	gtc	aac	acc	aca	tac	cag	ctc	cgg	gtc	agc	cgc	atg	gac	gat	ttt	545
Pro	Val	Asn	Thr	Thr	Tyr	Gln	Leu	Arg	Val	Ser	Arg	Met	Asp	Asp	Phe	
	140					145					150					
gtg	ctc	agg	act	ggg	gag	cag	ttc	agc	ttc	aat	acc	aca	gca	gca	cag	593
Val	Leu	Arg	Thr	Gly	Glu	Gln	Phe	Ser	Phe	Asn	Thr	Thr	Ala	Ala	Gln	
155					160					165					170	
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Pro	Gln	Tyr	Phe	Lys	Tyr	Glu	Phe	Pro	Glu	Gly	Val	Asp	Ser	Val	Ile	
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Val	Lys	Val	Thr	Ser	Asn	Lys	Ala	Phe	Pro	Cys	Ser	Val	Ile	Ser	Ile	
			190					195					200			
cag	gat	gtg	ctg	tgt	cct	gtc	tat	gac 652/		gac	aac	aac	gta	gcc	ttc	737

G1	n As	p Va	l Lei	Cys	Pro	Val	Tyr	Asp	Leu	Asp	Asn	Asn	Val	Ala	Phe	
		20	5				210	)				215	;			
at	c gg	c at	g tac	cag	acg	atg	acc	aag	aag	gcg	gcc	atc	acc	gta	cag	785
			t Tyr											_	_	
	22					225		-	-		230					
											200					
Cg	. aa	а дас	ttc	ccc	agc	aac	agc	ttt	tat	σtσ	σtσ	ata	ata	a+a	220	833
			Phe													000
23		,		110	240		501	THE	171	245		vai	741	141	•	
20.	,				240					240					250	
	~~				<b>.</b>			<b>.</b>	_ #			<b>.</b>				007
			caa												_	881
1 11 1	. GI	ı ASP	Gln		cys	GIÀ	стх	Ser		Pro	Pne	lyr	Pro		Ala	
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			ccg													929
Glı	ı Ası	Glu	Pro	Val	Asp	Gln	Gly	His	Arg	Gln	Lys	Thr	Leu	Ser	Val	
			270					275					280			
ctg	gte	tct	caa	gca	gtc	acg	tct	gag	gca	tac	gtc	agt	ggg	atg	ctc	977
Leu	Va]	Ser	Gln	Ala	Val	Thr	Ser	Glu	Ala	Tyr	Val	Ser	Gly	Met	Leu	
		285					290					295				
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Phe	Cys	Leu	Gly	Ile	Phe	Leu	Ser	Phe	Tyr	Leu	Leu	Thr	Val	Leu	Leu	
	300	)				305					310					
gcc	tgo	tgg	gag	aac	tgg	agg	cag	aag	aag	aag	acc	ctg	ctg	gtg	gcc	1073
Ala	Cys	Trp	Glu	Asn	Trp	Arg	Gln	Lys	Lys	Lys	Thr	Leu	Leu	Val	Ala	
								653/								

V	V <b>O</b> 02	/0537	37												PCT/J	Γ <b>P</b> 01/11389
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Ile	Asp	Arg	Ala	Cys	Pro	Glu	Ser	Gly	His	Pro	Arg	Val	Leu	Ala	Asp	
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tct	ttt	cct	ggc	agt	tcc	cct	tat	gag	ggt	tac	aac	tat	ggc	tcc	ttt	1169
Ser	Phe	Pro	Gly	Ser	Ser	Pro	Tyr	Glu	Gly	Tyr	Asn	Tyr	Gly	Ser	Phe	
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G1u	Asn	Val	Ser	Gly	Ser	Thr	Asp	Gly	Leu	Val	Asp	Ser	Ala	Gly	Thr	
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									tgc							1313
	Pro	Ser	Gly	Gln	Met	Arg	Gln	Leu	Cys	Ile	Ala	Met	Gly	Arg	Ser	
395					400					405					410	
									gtg							1361
Phe	Glu	Pro	Val		Thr	Arg	Pro	Arg	Val	Asp	Ser	Met	Ser	Ser	Val	
				415					420					425		
																w 4a -
									gac				_			1409
olu	Glu			Tyr	Asp	Thr	Leu		Asp	lle	Asp	Ser	_	Lys	Asn	
			430					435					440			

gt	c att	cgc	acc	aag	caa	tac	ctc	tat	gtg	gct	gac	ctg	gca	cgg	aag	1457
Va:	l Ile	Arg	Thr	Lys	G1n	Tyr	Leu	Tyr	Val	Ala	Asp	Leu	Ala	Arg	Lys	
		445					450					455				
gao	aag	cgt	gtt	ctg	cgg	aaa	aag	tac	cag	atc	tac	ttc	tgg	aac	att	1505
Asp	Lys	Arg	Val	Leu	Arg	Lys	Lys	Tyr	Gln	Ile	Tyr	Phe	Trp	Asn	Ile	
	460					465					470					
gco	acc	att	gct	gtc	ttc	tat	gcc	ctt	cct	gtg	gtg	cag	ctg	ete	atc	1553
	Thr													_		
475					480	-,-				485			200	,	490	
					200					100					100	
	+00			-+-	~+~	+	~+ <b>~</b>						_ 4 _		4	1.001
	tac															1601
ini	Tyr	GIN	ınr		vai	Asn	val	ınr		Asn	GIn	Asp	116		Tyr	
				495					500					505		
tac	aac	ttc	ctc	tgc	gcc	cac	cca	ctg	ggc	aat	ctc	agc	gcc	ttc	aac	1649
Tyr	Asn	Phe	Leu	Cys	Ala	His	Pro	Leu	Gly	Asn	Leu	Ser	Ala	Phe	Asn	
			510					515					520			
aac	atc	ctc	agc	aac	ctg	ggg	tac	atc	ctg	ctg	ggg	ctg	ctt	ttc	ctg	1697
Asn	Ile	Leu	Ser	Asn	Leu	Gly	Tyr	Ile	Leu	Leu	G1y	Leu	Leu	Phe	Leu	
		525					530					535				
ctc	atc	atc	ctg	caa	cgg	gag	atc	aac	cac	aac	cgg	gcc	ctg	ctg	cgc	1745
	Ile															
	540					545					550				0	
	- 25					- 10					555					

aat	gac	ctc	tgt	gcc	ctg	gaa	tgt	ggg	atc	ccc	aaa	cac	ttt	ggg	ctt	1793
Asn	Asp	Leu	Cys	Ala	Leu	Glu	Cys	Gly	Ile	Pro	Lys	His	Phe	Gly	Leu	
555					560					565					570	
ttc	tac	gcc	atg	ggc	aca	gcc	ctg	atg	atg	gag	ggg	ctg	ctc	agt	gct	1841
Phe	Tyr	Ala	Met	Gly	Thr	Ala	Leu	Met	Met	Glu	Gly	Leu	Leu	Ser	Ala	
				575					580					585		
tgc	tat	cat	gtg	tgc	ccc	aac	tat	acc	aat	ttc	cag	ttt	gac	aca	tcg	1889
Cys	Tyr	His	Val	Cys	Pro	Asn	Tyr	Thr	Asn	Phe	Gln	Phe	Asp	Thr	Ser	
			590					595					600			
ttc	atg	tac	atg	atc	gcc	gga	ctc	tgc	atg	ctg	aag	ctc	tac	cag	aag	1937
Phe	Met	Tyr	Met	Ile	Ala	Gly	Leu	Cys	Met	Leu	Lys	Leu	Tyr	Gln	Lys	
		605					610					615				
cgg	cac	ccg	gac	atc	aac	gcc	agc	gcc	tac	agt	gcc	tac	gcc	tgc	ctg	1985
Arg		Pro	Asp	Ile	Asn		Ser	Ala	Tyr	Ser	Ala	Tyr	Ala	Cys	Leu	
	620					625					630					
								ctg								2033
	Ile	Val	Ile	Phe		Ser	Val	Leu	Gly		Val	Phe	Gly	Lys	-	
335					640					645					650	
								tcc						_		2081
lsn	Inr	Ala	Phe		lle	Vai	Phe	Ser		IIe	H1S	lle	lle		Thr	
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<b></b>	<b></b> -	_ 4				_4-	<b>_</b>	<b>4</b>				4				0100
ug	ctc	CTC	agc	acg	cag	CTC	ıat	tac 656/		ggc	cgg	cgg	aaa	ctg	gac	2129

Leu Leu Ser Thr Gln Leu Tyr Tyr Met Gly Arg Trp Lys Leu Asp

			670					675					680			
			Phe		cgc Arg			His								2177
		000					050					095				
cgg	cag	tgc	agc	ggg	ccg	ctc	tac	gtg	gac	cgc	atg	gtg	ctg	ctg	gtc	2225
Arg		Cys	Ser	Gly	Pro	Leu	Tyr	Val	Asp	Arg	Met	Val	Leu	Leu	Val	
	700					705					710					
atg	ggc	aac	gtc	atc	aac	tgg	tcg	ctg	gct	gcc	tat	ggg	ctt	atc	atg	2273
Met	Gly	Asn	Val	Ile	Asn	Trp	Ser	Leu	Ala	Ala	Tyr	Gly	Leu	Ile	Met	
715					720					725					730	•
								•								
					gct											2321
Arg	Pro	Asn	Asp		Ala	Ser	Tyr	Leu		Ala	Ile	Gly	Ile		Asn	
				735					740					745		
ctg	ctc	ctt	tac	ttc	gcc	ttc	tac	atc	atc	atg	aag	ctc	cgg	agt	ggg	2369
Leu	Leu	Leu	Tyr	Phe	Ala	Phe	Tyr	Ile	Ile	Met	Lys	Leu	Arg	Ser	Gly	
			750					<b>7</b> 55					760			
gag	agg	atc	aag	ctc	atc	ccc	ctg	ctc	tgc	atc	gtt	tgc	acc	tcc	gtg	2417
Hu	Arg		Lys	Leu	Ile	Pro	Leu	Leu	Cys	Ile	Val		Thr	Ser	Val	
		765					770					775				
gtc	tgg	ggc	ttc	gcg	ctc	ttc	ttc	ttc	ttc	cag	gga	ctc	agc	acc	tgg	2465
/al	Trp	G1y	Phe	Ala	Leu	Phe	Phe	Phe 657/		Gln	Gly	Leu	Ser	Thr	Trp	
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780 785 790 cag aaa acc cct gca gag tcg agg gag cac aac cgg gac tgc atc ctc 2513 Gln Lys Thr Pro Ala Glu Ser Arg Glu His Asn Arg Asp Cys Ile Leu 795 800 805 810 ctc gac ttc ttt gac gac cac gac atc tgg cac ttc ctc tcc atc 2561 Leu Asp Phe Phe Asp Asp His Asp Ile Trp His Phe Leu Ser Ser Ile 815 820 825 gcc atg ttc ggg tcc ttc ctg gta agc ggg cct ccc ggc cga gcc ggg 2609 Ala Met Phe Gly Ser Phe Leu Val Ser Gly Pro Pro Gly Arg Ala Gly 830 835 840 tgg gta cgt gaa ggt agc agc tgc ctc ctt ccc tgt ggc tgatctggcg 2658 Trp Val Arg Glu Gly Ser Ser Cys Leu Leu Pro Cys Gly 845 850 855 tccacacccc aggtgttgct gacactggat gacgacctgg atacttagaa aggggcttca 2718 ggaagggatg tgctgtttcc ctctacgtgc ccagtcctag cctcgctcta ggacccaggg 2778 ctggcttcta agtttccgtc cagtcttcag gcaagttctg tgttagtcat gcacacacat 2838 acctatgaaa cettggagtt tacaaagaat tgccccagct ctgggcaccc tggccaccct 2898

ggtccttgga tccccttcgt ccacctggt ccacccaga tgctgaggat gggggagctc 2958

aggoggggcc totgotttgg ggatgggaat gtgtttttct cccaaacttg tttttatagc 3018 658/735

tctgcttgaa gggctgggag atgaggtggg tctggatctt ttctcagagc gtctccatgc 3078

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<210> 166

<211> 855

<212> PRT

<213> Homo sapiens

<400> 166

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Glu Ser His Leu Gly Val Leu Gly Pro Lys Asn Val Ser Gln Lys Asp

20 25 30

Ala Glu Phe Glu Arg Thr Tyr Val Asp Glu Val Asn Ser Glu Leu Val

35 40 45

Asn Ile Tyr Thr Phe Asn His Thr Val Thr Arg Asn Arg Thr Glu Gly

50 55 60

85

Val Arg Val Ser Val Asn Val Leu Asn Lys Gln Lys Gly Ala Pro Leu

65 70 75 80

Leu Phe Val Val Arg Gln Lys Glu Ala Val Val Ser Phe Gln Val Pro

90 95

Leu	Ile	Leu	Arg	Gly	Met	Phe	Gln	Arg	Lys	Tyr	Leu	Tyr	Gln	Lys	Val
			100					105					110		
Glu	Arg	Thr	Leu	Cys	Gln	Pro	Pro	Thr	Lys	Asn	Glu	Ser	Glu	Ile	Gln
		115					120					125			
Phe	Phe	Tyr	Val	Asp	Val	Ser	Thr	Leu	Ser	Pro	Val	Asn	Thr	Thr	Tyr
	130					135					140			٠	
Gln	Leu	Arg	Val	Ser	Arg	Met	Asp	Asp	Phe	Val	Leu	Arg	Thr	Gly	Glu
145					150					155					160
Gln	Phe	Ser	Phe		Thr	Thr	Ala	Ala		Pro	G1n	Tyr	Phe	Lys	Tyr
				165					170					175	
Glu	Phe	Pro		Gly	Val	Asp	Ser		Ile	Val	Lys	Val		Ser	Asn
			180					185					190		
Lys	Ala		Pro	Cys	Ser	Val		Ser	Ile	Gln	Asp		Leu	Cys	Pro
		195					200					205			
Val	Tyr	Asp	Leu	Asp	Asn		Val	Ala	Phe	Ile		Met	Tyr	Gln	Thr
	210					215					220				
	Thr	Lys	Lys	Ala		Ile	Thr	Val	Gln		Lys	Asp	Phe	Pro	Ser
225					230					235					240
Asn	Ser	Phe	Tyr	Val	Val	Val	Val	Val 660/	-	Thr	Glu	Asp	Gln	Ala	Cys

245 250 255

Gly Gly Ser Leu Pro Phe Tyr Pro Phe Ala Glu Asp Glu Pro Val Asp
260 265 270

Gln Gly His Arg Gln Lys Thr Leu Ser Val Leu Val Ser Gln Ala Val 275 280 285

Thr Ser Glu Ala Tyr Val Ser Gly Met Leu Phe Cys Leu Gly Ile Phe 290 295 300

Leu Ser Phe Tyr Leu Leu Thr Val Leu Leu Ala Cys Trp Glu Asn Trp 305 310 315 320

Arg Gln Lys Lys Thr Leu Leu Val Ala Ile Asp Arg Ala Cys Pro 325 330 335

Glu Ser Gly His Pro Arg Val Leu Ala Asp Ser Phe Pro Gly Ser Ser 340 345 350

Pro Tyr Glu Gly Tyr Asn Tyr Gly Ser Phe Glu Asn Val Ser Gly Ser 355 360 365

Thr Asp Gly Leu Val Asp Ser Ala Gly Thr Gly Asp Leu Ser Tyr Gly 370 375 380

Tyr Gln Gly His Asp Gln Phe Lys Arg Arg Leu Pro Ser Gly Gln Met 385 390 395 400

Arg	G1n	Leu	Cys	Ile 405	Ala	Met	Gly	Arg	Ser 410	Phe	Glu	Pro	Val	Gly 415	Thr
Arg	Pro	Arg	Val 420	Asp	Ser	Met	Ser	Ser 425	Val	Glu	Glu	Asp	Asp 430	Tyr	Asp
Thr	Leu	Thr 435	Asp	Ile	Asp	Ser	Asp 440	Lys	Asn	Val	Ile	Arg 445	Thr	Lys	Gln
Tyr	Leu 450	Tyr	Val	Ala	Asp	Leu 455	Ala	Arg	Lys	Asp	Lys 460	Arg	Val	Leu	Arg
Lys 465	Lys	Tyr	G1n	Ile	Tyr 470	Phe	Trp	Asn	Ile	Ala 475	Thr	Ile	Ala	Val	Phe 480
Tyr	Ala	Leu	Pro	Val 485	Val	Gln	Leu	Val	Ile 490	Thr	Tyr	Gln	Thr	Val 495	Val
Asn	Val	Thr	Gly 500	Asn	Gln	Asp	Ile	Cys 505	Tyr	Tyr	Asn	Phe	Leu 510	Cys	Ala
His	Pro	Leu 515	Gly	Asn	Leu	Ser	Ala 520	Phe	Asn	Asn	Ile	Leu 525	Ser	Asn	Leu
Gly	Tyr 530	Ile	Leu	Leu	Gly	Leu 535	Leu	Phe	Leu	Leu	Ile 540	Ile	Leu	Gln	Arg

Glu Ile Asn His Asn Arg Ala Leu Leu Arg Asn Asp Leu Cys Ala Leu 545 550 550 555 555 560

Glu	Cys	Gly	Ile	Pro	Lys	His	Phe	Gly	Leu	Phe	Tyr	Ala	Met	Gly	Thr
				<b>56</b> 5					570					575	

- Ala Leu Met Met Glu Gly Leu Leu Ser Ala Cys Tyr His Val Cys Pro 580 585 590
- Asn Tyr Thr Asn Phe Gln Phe Asp Thr Ser Phe Met Tyr Met Ile Ala 595 600 605
- Gly Leu Cys Met Leu Lys Leu Tyr Gln Lys Arg His Pro Asp Ile Asn 610 615 620
- Ala Ser Ala Tyr Ser Ala Tyr Ala Cys Leu Ala Ile Val Ile Phe Phe 625 630 635 640
- Ser Val Leu Gly Val Val Phe Gly Lys Gly Asn Thr Ala Phe Trp Ile 645 650 655
- Val Phe Ser Ile Ile His Ile Ile Ala Thr Leu Leu Leu Ser Thr Gln 660 665 670
- Leu Tyr Tyr Met Gly Arg Trp Lys Leu Asp Ser Gly Ile Phe Arg Arg 675 680 685
- Ile Leu His Val Leu Tyr Thr Asp Cys Ile Arg Gln Cys Ser Gly Pro 690 695 700
- Leu Tyr Val Asp Arg Met Val Leu Leu Val Met Gly Asn Val Ile Asn 663/735

705 710 715 720

Trp Ser Leu Ala Ala Tyr Gly Leu IIe Met Arg Pro Asn Asp Phe Ala
725 730 735

Ser Tyr Leu Leu Ala Ile Gly Ile Cys Asn Leu Leu Leu Tyr Phe Ala 740 745 750

Phe Tyr Ile Ile Met Lys Leu Arg Ser Gly Glu Arg Ile Lys Leu Ile
755 760 765

Pro Leu Cys Ile Val Cys Thr Ser Val Val Trp Gly Phe Ala Leu 770 775 780

Phe Phe Phe Gln Gly Leu Ser Thr Trp Gln Lys Thr Pro Ala Glu
785 790 795 800

Ser Arg Glu His Asn Arg Asp Cys Ile Leu Leu Asp Phe Phe Asp Asp 805 810 815

His Asp Ile Trp His Phe Leu Ser Ser Ile Ala Met Phe Gly Ser Phe 820 825 830

Leu Val Ser Gly Pro Pro Gly Arg Ala Gly Trp Val Arg Glu Gly Ser 835 840 845

Ser Cys Leu Leu Pro Cys Gly 850 855

<210> 167

<211> 2815

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (56).. (571)

5

<400> 167

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Met

1

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Arg Arg Gln Pro Ala Lys Val Ala Ala Leu Leu Leu Gly Leu Leu Leu

10 15

gag tgc aca gaa gcc aaa aag cat tgc tgg tat ttc gaa gga ctc tat 154 Glu Cys Thr Glu Ala Lys Lys His Cys Trp Tyr Phe Glu Gly Leu Tyr

20 25 30

cca acc tat tat ata tgc cgc tcc tac gag gac tgc tgt ggc tcc agg 202

Pro Thr Tyr Tyr Ile Cys Arg Ser Tyr Glu Asp Cys Cys Gly Ser Arg

35 40 45

tgc tgt gtg cgg gcc ctc tcc ata cag agg ctg tgg tac ttc tgg ttc 250 665/735

Cys	Cys	Val	Arg	Ala	Leu	Ser	Ile	Gln	Arg	Leu	Trp	Tyr	Phe	Trp	Phe	
50					55					60					65	
ctt	ctg	atg	atg	ggc	gtg	ctt	ttc	tgc	tgc	gga	gcc	ggc	ttc	ttc	atc	298
Leu	Leu	Met	Met	Gly	Val	Leu	Phe	Cys	Cys	Gly	Ala	Gly	Phe	Phe	Ile	
				70					75					80		
cgg	agg	cgc	atg	tac	ccc	ccg	ccg	ctg	atc	gag	gag	cca	gcc	ttc	aat	346
Arg	Arg	Arg	Met	Tyr	Pro	Pro	Pro	Leu	Ile	Glu	Glu	Pro	Ala	Phe	Asn	
			85					90					95			
gtg	tcc	tac	acc	agg	cag	ccc	cca	aat	ccc	ggc	cca	gga	gcc	cag	cag	394
Val	Ser	Tyr	Thr	Arg	Gln	Pro	Pro	Asn	Pro	Gly	Pro	Gly	Ala	Gln	Gln	
		100					105					110				
ccg	ggg	ccg	ccc	tat	tac	acc	gac	cca	gga	gga	ccg	ggg	atg	aac	cct	442
Pro	Gly	Pro	Pro	Tyr	Tyr	Thr	Asp	Pro	G1y	Gly	Pro	Gly	Met	Asn	Pro	
	115					120					125					
gtc	ggg	aat	tcc	atg	gca	atg	gct	ttc	cag	gtc	cca	ccc	aac	tca	ccc	490
Val	Gly	Asn	Ser	Met	Ala	Met	Ala	Phe	G1n	Val	Pro	Pro	Asn	Ser	Pro	
130					135					140					145	
cag	ggg	agt	gtg	gcc	tgc	ccg	ccc	cct	cca	gcc	tac	tgc	aac	acg	cct	538
Gln	Gly	Ser	Val	Ala	Cys	Pro	Pro	Pro	Pro	Ala	Tyr	Cys	Asn	Thr	Pro	
				150					155					160		
ccg	ссс	ccg	tac	gaa	cag	gta	gtg	aag	gcc	aag	tagt	gggg	gtg c	ccac	gtgca	591
Pro	Pro	Pro	Tyr	Glu	Gln	Val	Val	Lys	Ala	Lys						

165 170

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eagagtaaae ttgaageaga tetgtgeatg etttteetet geaacaattg getegttet 2751
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<210> 168

<211> 172

<212> PRT

<213> Homo sapiens

<400> 168

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1 5 10 15
669/735

Leu	Glu	Cys	Thr	Glu	Ala	Lys	Lys	His	Cys	Trp	Tyr	Phe	Glu	G1y	Leu
			20					25					30		
Т	D	Th	Т	Т	T1.	C	A	C	Т	C1	A	C	C	· 01	C
ıyr	Pro		lyr	lyr	116	Cys		Ser	ıyr	GIU	Asp		Cys	GIA	Ser
		35					40					45			
Arg	Cys	Cys	Val	Arg	Ala	Leu	Ser	Ile	Gln	Arg	Leu	Tro	Tyr	Phe	Trp
	50					55					60		-,-		
Phe	Leu	Leu	Met	Met	Gly	Val	Leu	Phe	Cys	Cys	Gly	Ala	Gly	Phe	Phe
65					70					75					80
Ile	Arg	Arg	Arg	Met	Tyr	Pro	Pro	Pro	Leu	Ile	Glu	Glu	Pro	Ala	Phe
				85					90					95	
Asn	Val	Ser	Tyr	Thr	Arg	Gln	Pro	Pro	Asn	Pro	Gly	Pro	Gly	Ala	Gln
			100					105					110		
Gln	Pro	G1y	Pro	Pro	Tyr	Tyr	Thr	Asp	Pro	Gly	Gly	Pro	Gly	Met	Asn
		115					120					125			
Pro	Val	Gly	Asn	Ser	Met	Ala	Met	Ala	Phe	G1n	Val	Pro	Pro	Asn	Ser
	130					135					140				
Pro	G1n	Gly	Ser	Val	Ala	Cys	Pro	Pro	Pro	Pro	Ala	Tyr	Cys	Asn	Thr
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Pro	Pro	Pro	Pro	Tyr	G1u	Gln	Val	Val	Lys	Ala	Lys				

165 170

<210> 169

<211> 3337

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (136).. (1755)

<400> 169

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taccegagte tegttteete teagteeate caccetteat ggggeeagag ceetetetee 120

agaatctgag cagca atg ccg ttt gct gaa gac aag acc tat aag tat atc 171

Met Pro Phe Ala Glu Asp Lys Thr Tyr Lys Tyr Ile

1 5 10

tgc cgc aat ttc agc aat ttt tgc aat gtg gat gtt gta gag att ctg 219 Cys Arg Asn Phe Ser Asn Phe Cys Asn Val Asp Val Val Glu Ile Leu

15 20 25

cct tac ctg ccc tgc ctc aca gca aga gac cag gat cga ctg cgg gcc 267
Pro Tyr Leu Pro Cys Leu Thr Ala Arg Asp Gln Asp Arg Leu Arg Ala

30 35 40

acc	tgc	aca	ctc	tca	ggg	aac	cgg	gac	acc	ctc	tgg	cat	ctc	ttc	aat	315
Thr	Cys	Thr	Leu	Ser	Gly	Asn	Arg	Asp	Thr	Leu	Trp	His	Leu	Phe	Asn	
45					50					55					60	
acc	ctt	cag	cgg	cgg	ccc	ggc	tgg	gtg	gag	tac	ttc	att	gcg	gca	ctg	363
Thr	Leu	Gln	Arg	Arg	Pro	Gly	Trp	Val	Glu	Tyr	Phe	Ile	Ala	Ala	Leu	
				65					70					75		
agg	ggc	tgt	gag	cta	gtt	gat	ctc	gcg	gac	gaa	gtg	gcc	tct	gtc	tac	411
Arg	Gly	Cys	Glu	Leu	Val	Asp	Leu	Ala	Asp	Glu	Val	Ala	Ser	Val	Tyr	
			80					85					90			
_	_		cag					_	_			_		_		459
G1n	Ser		Gln	Pro	Arg	Thr		Asp	Arg	Pro	Pro	-		Leu	Glu	
		95					100					105				
			ctt		_											507
Pro		Ser	Leu	Pro	Ala		Arg	Pro	Gly	Pro		Thr	Pro	Ala	Ala	
	110					115					120					
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			atc													555
	птѕ	SeT	Ile	FIO		ASII	Ser	Cys	MIR		Lys	GIU	Pro	ser	-	
125					130					135					140	
ccc	ato	cct	gtc	csa	gag	acc	caa	aca	cca	gag	tcc	CCS	aas	ao a	22+	603
			Val													003
-10	11100	0	,41	145	JIU	1111	0111	1110	150	Jiu	501		оту	155	uoli	
				110					100					100		

tca	gag	caa	gcc	ctg	cag	acg	ctc	agc	ccc	aga	gcc	atc	cca	agg	aat	651
Ser	Glu	Gln	Ala	Leu	Gln	Thr	Leu	Ser	Pro	Arg	Ala	Ile	Pro	Arg	Asn	
			160					165					170			
cca	gat	ggt	ggc	ссс	ctg	gag	tcc	tcc	tct	gac	ctg	gca	gcc	ctc	agc	699
Pro	Asp	Gly	Gly	Pro	Leu	G1u	Ser	Ser	Ser	Asp	Leu	Ala	Ala	Leu	Ser	
		175					180					185				
cct	ctg	acc	tcc	agc	ggg	cat	cag	gag	cag	gac	aca	gaa	ctg	ggc	agt	747
		Thr														
	190					195				_	200					
acc	cac	aca	gca	ggt	gcg	acc	tcc	agc	ctc	aca	cca	tcc	cgt	ggg	cct	795
		Thr														
205				,	210					215		551		01)	220	
															220	
øtø	tet	cca	tet	gtc	tee	ttc	cag	ccc	cto	gcc.	cat	tcc	acc	ccc	200	843
		Pro														040
741	Der	110	Der		561	1 116	OIII	110		ліа	VI R	SeI	1111		мg	
				225					230					235		
		cgc														891
Ala	Ser	Arg		Pro	Gly	Pro	Thr		Ser	Val	Val	Ser		Gly	Thr	
			240					245					250			
tcc	ttc	tcc	tcc	tca	tcc	cct	ggc	ttg	gcc	tct	gca	ggg	gct	gca	gag	939
Ser	Phe	Ser	Ser	Ser	Ser	Pro	G1y	Leu	Ala	Ser	Ala	Gly	Ala	Ala	Glu	
		255					260					265				
ggt	aaa	cag	ggt	gca	gag	agt	gac	cag	gcc	gag	cct	atc	atc	tgc	tcc	987
								673/	735							

Gly Lys Gln Gly Ala Glu Ser Asp Gln Ala Glu Pro Ile Ile Cys Ser agt ggg gca gag gca cct gcc aac tct ctg ccc tcc aaa gtg cct acc Ser Gly Ala Glu Ala Pro Ala Asn Ser Leu Pro Ser Lys Val Pro Thr acc ttg atg cct gtg aac aca gtg gcc ctg aaa gtg cct gcc aac cca Thr Leu Met Pro Val Asn Thr Val Ala Leu Lys Val Pro Ala Asn Pro gca tct gtc agc aca gtg ccc tcc aag ttg cca act agc tca aag ccc Ala Ser Val Ser Thr Val Pro Ser Lys Leu Pro Thr Ser Ser Lys Pro cct ggt gca gtg cct tct aat gcg ctc acc aat cca gca cca tcc aaa Pro Gly Ala Val Pro Ser Asn Ala Leu Thr Asn Pro Ala Pro Ser Lys ttg ccc atc aac tca acc cgt gct ggc atg gtg cca tcc aaa gtg cct Leu Pro Ile Asn Ser Thr Arg Ala Gly Met Val Pro Ser Lys Val Pro act agc atg gtg ctc acc aag gtg tct gcc agc aca gtc ccc act gac Thr Ser Met Val Leu Thr Lys Val Ser Ala Ser Thr Val Pro Thr Asp ggg agc agc aga aat gag gag acc cca gca gct cca aca ccc gcc ggc Gly Ser Ser Arg Asn Glu Glu Thr Pro Ala Ala Pro Thr Pro Ala Gly 674/735

gcc act gga ggc agc tca gcc tgg cta gac agc agc tct gag aat agg Ala Thr Gly Gly Ser Ser Ala Trp Leu Asp Ser Ser Ser Glu Asn Arg ggc ctt ggg tcg gag ctg agt aag cct ggc gtg ctg gca tcc cag gta Gly Leu Gly Ser Glu Leu Ser Lys Pro Gly Val Leu Ala Ser Gln Val gac agc ccg ttc tcg ggc tgc ttc gag gat ctt gcc atc agt gcc agc Asp Ser Pro Phe Ser Gly Cys Phe Glu Asp Leu Ala Ile Ser Ala Ser acc tcc ttg ggc atg ggg ccc tgc cat ggc cca gag gag aat gag tat Thr Ser Leu Gly Met Gly Pro Cys His Gly Pro Glu Glu Asn Glu Tyr aag too gag ggc acc ttt ggg atc cac gtg gct gag aac ccc agc atc Lys Ser Glu Gly Thr Phe Gly Ile His Val Ala Glu Asn Pro Ser Ile cag ctc ctg gag ggc aac cct ggg cca cct gcg gac ccg gat ggc ggc Gln Leu Leu Glu Gly Asn Pro Gly Pro Pro Ala Asp Pro Asp Gly Gly

ccc agg cca caa gcc gac cgg aag ttc cag gag agg gag gtg cca tgc1659Pro Arg Pro Gln Ala Asp Arg Lys Phe Gln Glu Arg Glu Val Pro Cys495500505

cac agg ccc tca cct ggg gct ctg tgg ctc cag gtg gct gtg aca ggg 1707 His Arg Pro Ser Pro Gly Ala Leu Trp Leu Gln Val Ala Val Thr Gly 510 515 520

gtg ctg gta gtc aca ctc ctg gtg gtg ctg tac cgg cgg cgt ctg cac 1755

Val Leu Val Val Thr Leu Leu Val Val Leu Tyr Arg Arg Arg Leu His

525 530 535 540

tagtgaagce etgggetett eccaecacce atetgtteeg tteetgeagt atacetggee 1815
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ggetggggag gagacacetg gtgggeagag eteaggeaga ggtttggatt teageteect 1935
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taggtaccca tgctgggcag gtcagttaac aatttatgca caggtactag ttttattgta 3315

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3337

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<211> 540

<212> PRT

<213> Homo sapiens

<400> 170

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Ser Asn Phe Cys Asn Val Asp Val Val Glu Ile Leu Pro Tyr Leu Pro
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Cys Leu Thr Ala Arg Asp Gln Asp Arg Leu Arg Ala Thr Cys Thr Leu 35 40 45

Ser Gly Asn Arg Asp Thr Leu Trp His Leu Phe Asn Thr Leu Gln Arg
50 55 60

Arg Pro Gly Trp Val Glu Tyr Phe Ile Ala Ala Leu Arg Gly Cys Glu 65 70 75 80

Leu Val Asp Leu Ala Asp Glu Val Ala Ser Val Tyr Gln Ser Tyr Gln

85 90 95

678/735

Pro	Arg	Thr	Ser	Asp	Arg	Pro	Pro	Asp	Pro	Leu	G1u	Pro	Pro	Ser	Leu
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Pro	Ala	Glu 115	Arg	Pro	Gly	Pro	Pro 120	Thr	Pro	Ala	Ala	Ala 125	His	Ser	Ile
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Pro	Tyr _.	Asn	Ser	Cys	Arg	Glu	Lys	Glu	Pro	Ser	Tyr	Pro	Met	Pro	Val
	130					135					140				
G1n	Glu	Thr	G1n	Ala	Pro	Glu	Ser	Pro	Glv	Glu	Asn	Ser	Glu	G1n	Ala
145	014				150	020	001	•••	01,	155		202	014		160
Leu	Gln	Thr	Leu	Ser	Pro	Arg	Ala	Ile	Pro	Arg	Asn	Pro	Asp	Gly	Gly
				165					170					175	
Pro	Leu	Glu	Ser	Ser	Ser	Asp	Leu	Ala	Ala	Leu	Ser	Pro	Leu	Thr	Ser
			180					185					190		
Ser	G1y		Gln	Glu	Gln	Asp		Glu	Leu	Gly	Ser		His	Thr	Ala
		195					200					205			
Gly	Ala	Thr	Ser	Ser	Leu	Thr	Pro	Ser	Arg	G1y	Pro	Va1	Ser	Pro	Ser
	210					215					220				
	Ser	Phe	Gln	Pro		Ala	Arg	Ser	Thr		Arg	Ala	Ser	Arg	
225					230					235					240
Pro	Gly	Pro	Thr	Gly	Ser	Val	Val	Ser	Thr	Gly	Thr	Ser	Phe	Ser	Ser

245 250 255

Ser Ser Pro Gly Leu Ala Ser Ala Gly Ala Ala Glu Gly Lys Gln Gly
260 265 270

Ala Glu Ser Asp Gln Ala Glu Pro Ile Ile Cys Ser Ser Gly Ala Glu 275 280 285

Ala Pro Ala Asn Ser Leu Pro Ser Lys Val Pro Thr Thr Leu Met Pro 290 295 300

Val Asn Thr Val Ala Leu Lys Val Pro Ala Asn Pro Ala Ser Val Ser 305 310 315 320

Thr Val Pro Ser Lys Leu Pro Thr Ser Ser Lys Pro Pro Gly Ala Val 325 330 335

Pro Ser Asn Ala Leu Thr Asn Pro Ala Pro Ser Lys Leu Pro Ile Asn 340 345 350

Ser Thr Arg Ala Gly Met Val Pro Ser Lys Val Pro Thr Ser Met Val
355 360 365

Leu Thr Lys Val Ser Ala Ser Thr Val Pro Thr Asp Gly Ser Ser Arg 370 375 380

Asn Glu Glu Thr Pro Ala Ala Pro Thr Pro Ala Gly Ala Thr Gly Gly 385 390 395 400

Ser Ser Ala Trp Leu Asp Ser Ser Ser Glu Asn Arg Gly Leu Gly Ser
405 410 415

Glu Leu Ser Lys Pro Gly Val Leu Ala Ser Gln Val Asp Ser Pro Phe 420 425 430

Ser Gly Cys Phe Glu Asp Leu Ala Ile Ser Ala Ser Thr Ser Leu Gly
435 440 445

Met Gly Pro Cys His Gly Pro Glu Glu Asn Glu Tyr Lys Ser Glu Gly
450 455 460

Thr Phe Gly Ile His Val Ala Glu Asn Pro Ser Ile Gln Leu Leu Glu 465 470 475 480

Gly Asn Pro Gly Pro Pro Ala Asp Pro Asp Gly Gly Pro Arg Pro Gln
485 490 495

Ala Asp Arg Lys Phe Gln Glu Arg Glu Val Pro Cys His Arg Pro Ser 500 505 510

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Thr Leu Leu Val Val Leu Tyr Arg Arg Arg Leu His
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Ala Ala Arg Gln Leu Gly Leu Leu Val Asp Leu Ser Pro Asp Gly Leu
20 25 30

atg atc cct gag gac ggg gct aac gat gaa gaa ctg gag gct gag ttc 385 Met Ile Pro Glu Asp Gly Ala Asn Asp Glu Glu Leu Glu Ala Glu Phe

35 40 45

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Leu	Ala	Leu	Val	Gly	Gly	Gln	Pro	Pro	Ala	Leu	Glu	Lys	Leu	Lys	Gly	
	50					55					60					
aaa	ggt	ccc	ttg	ccg	atg	gag	gcc	att	gag	aag	atg	gcc	agc	ctg	tgc	481
Lys	Gly	Pro	Leu	Pro	Met	Glu	Ala	Ile	Glu	Lys	Met	Ala	Ser	Leu	Cys	
65					70					75					80	
atg	aga	gac	ccg	gat	gag	gat	gag	gag	gag	ggg	acg	gat	gag	gac	gac	529
Met	Arg	Asp	Pro	Asp	Glu	Asp	Glu	G1u	Glu	Gly	Thr	Asp	Glu	Asp	Asp	
				85					90					95		
ttg	gag	gct	gat	gat	gac	ctg	ctg	gcg	gag	cta	aat	gag	gtc	cţt	gga	577
Leu	Glu	Ala	Asp	Asp	Asp	Leu	Leu	Ala	Glu	Leu	Asn	Glu	Val	Leu	Gly	
			100					105					110			
gag	gag	cag	aag	gct	tca	gag	acc	cca	cct	cct	gtg	gcc	cag	ccg	aag	625
Glu	Glu	G1n	Lys	Ala	Ser	Glu	Thr	Pro	Pro	Pro	Val	Ala	Gln	Pro	Lys	
		115					120					125				
cct	gag	gcc	cct	cat	ccg	ggg	ctg	gag	acc	acc	ttg	cag	gag	agg	ctg	673
Pro	Glu	Ala	Pro	His	Pro	Gly	Leu	Glu	Thr	Thr	Leu	Gln	G1u	Arg	Leu	
	130					135					140					
gcg	ctc	tat	cag	aca	gca	att	gaa	agc	gcc	aga	caa	gct	gga	gac	agc	721
Ala	Leu	Tyr	Gln	Thr	Ala	Ile	Glu	Ser	Ala	Arg	Gln	Ala	Gly	Asp	Ser	
145					150					155					160	

gc	c aag	atg	cgg	cgc	tac	gat	cgg	ggg	ctt	aaa	aca	ctg	gaa	aac	ctg	769
Ala	a Lys	Met	Arg	Arg	Tyr	Asp	Arg	Gly	Leu	Lys	Thr	Leu	Glu	Asn	Leu	
				165					170					175		
cto	gcc	tcc	atc	cgt	aag	ggc	aat	gcc	att	gac	gaa	gcg	gac	atc	ccg	817
Lei	ı Ala	Ser	Ile	Arg	Lys	Gly	Asn	Ala	Ile	Asp	Glu	Ala	Asp	Ile	Pro	
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CCE	д сса	gtg	gcc	ata	gga	aaa	ggc	ccg	gcg	tcc	acg	cct	acc	tac	agc	865
Pro	Pro	Val	Ala	Ile	Gly	Lys	Gly	Pro	Ala	Ser	Thr	Pro	Thr	Tyr	Ser	
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cct	gca	ссс	acc	cag	ccg	gcc	cct	aga	atc	gcg	tca	gcc	cca	gag	ссс	913
Pro	Ala	Pro	Thr	G1n	Pro	Ala	Pro	Arg	Ile	Ala	Ser	Ala	Pro	G1u	Pro	
	210					215					220					
agg	gtc	acc	ctg	gag	gga	cct	tct	gcc	acc	gcc	cca	gcc	tca	tct	cca	961
Arg	. Val	Thr	Leu	G1u	Gly	Pro	Ser	Ala	Thr	Ala	Pro	Ala	Ser	Ser	Pro	
225	;				230					235					240	
ggc	ttg	gct	aag	ссс	cag	atg	ссс	cca	ggt	ccc	tgc	agc	cct	ggc	cct	1009
Gly	Leu	Ala	Lys	Pro	Gln	Met	Pro	Pro	Gly	Pro	Cys	Ser	Pro	Gly	Pro	
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ctg	gcc	cag	ttg	cag	agc	cgc	cag	cgc	gac	tac	aag	ctg	gct	gcc	ctc	1057
Leu	Ala	Gln	Leu	Gln	Ser	Arg	Gln	Arg	Asp	Tyr	Lys	Leu	Ala	Ala	Leu	
			260					265					270			
cac	gcc	aag	cag	cag	gga	gat	acc	act	gct	gcc	gct	aga	cac	ttc	cgc	1105
								684/	735							

His Ala Lys Gln Gln Gly Asp Thr Thr Ala Ala Ala Arg His Phe Arg gtg gct aag agc ttt gat gct gtc ttg gag gcc ctg agc cgg ggt gag Val Ala Lys Ser Phe Asp Ala Val Leu Glu Ala Leu Ser Arg Gly Glu ccc gtg gac ctc tcc tgc ctg ccc cct cca ccc gac cag ctg ccc cca Pro Val Asp Leu Ser Cys Leu Pro Pro Pro Pro Asp Gln Leu Pro Pro gac cca ccg tca cca ccg tcg cag cct ccg acc ccc gct acg gcg ccc Asp Pro Pro Ser Pro Pro Ser Gln Pro Pro Thr Pro Ala Thr Ala Pro tcc aca aca gag gtg ccc cca ccc ccg agg acc ctg ctg gag gcg ctg Ser Thr Thr Glu Val Pro Pro Pro Pro Arg Thr Leu Leu Glu Ala Leu gag cag cgg atg gag cgg tac cag gtg gcc gca gcc cag gcc aag agc Glu Gln Arg Met Glu Arg Tyr Gln Val Ala Ala Ala Gln Ala Lys Ser aag ggg gac cag cgg aaa gct cga atg cac gag cgc atc gtc aag caa Lys Gly Asp Gln Arg Lys Ala Arg Met His Glu Arg Ile Val Lys Gln tac caa gat gcc atc cga gcc cac aag gct ggc cga gcc gtg gat gtc Tyr Gln Asp Ala Ile Arg Ala His Lys Ala Gly Arg Ala Val Asp Val 685/735

gct gaa ttg ccc gtg ccc cca ggc ttc ccc cca atc cag ggc ctg gag Ala Glu Leu Pro Val Pro Pro Gly Phe Pro Pro Ile Gln Gly Leu Glu gcc acc aag ccc acc cag cag agt ctg gtg ggt gtc ctg gag act gcc Ala Thr Lys Pro Thr Gln Gln Ser Leu Val Gly Val Leu Glu Thr Ala atg aag ctg gcc aac cag gat gaa ggc cca gag gat gaa gag gat gag Met Lys Leu Ala Asn Gln Asp Glu Gly Pro Glu Asp Glu Glu Asp Glu gtg cct aag aag cag aac agc cct gtg gcc ccc aca gcc cag ccc aaa Val Pro Lys Lys Gln Asn Ser Pro Val Ala Pro Thr Ala Gln Pro Lys gcc cca ccc tca aga act ccc cag tcg gga tca gcc cca aca gcc aaa Ala Pro Pro Ser Arg Thr Pro Gln Ser Gly Ser Ala Pro Thr Ala Lys gcg ccc ccc aaa gcc aca tcc acc aga gcc cag cag cag ctg gcc ttc Ala Pro Pro Lys Ala Thr Ser Thr Arg Ala Gln Gln Gln Leu Ala Phe cta gag ggc cgc aag aag cag ctc ctg cag gcc gca ctg cga gcc aag Leu Glu Gly Arg Lys Lys Gln Leu Leu Gln Ala Ala Leu Arg Ala Lys

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WO 02/053737

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Gln	Lys	Asn	Asp	Val	Glu	Gly	Ala	Lys	Met	His	Leu	Arg	Gln	Ala	Lys	
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gga	ctg	gag	cct	atg	ctg	gag	gcc	tcg	cgc	aat	ggg	ctg	cct	gtg	gac	1873
Gly	Leu	Glu	Pro	Met	Leu	Glu	Ala	Ser	Arg	Asn	Gly	Leu	Pro	Val	Asp	
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atc	acc	aag	gtg	ccg	cct	gcc	cct	gtc	aac	aag	gac	gac	ttt	gcc	ctg	1921
Ile	Thr	Lys	Val	Pro	Pro	Ala	Pro	Val	Asn	Lys	Asp	Asp	Phe	Ala	Leu	
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Val	Gln	Arg	Pro	G1y	Pro	G1y	Leu	Ser	G1n	G1u	Ala	Ala	Arg	Arg	Tyr	
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							•									
ggt	gaa	ctc	acc	aag	ctc	ata	cgg	cag	cag	cac	gag	atg	tgc	ctg	aac	2017
G1y	Glu	Leu	Thr	Lys	Leu	Ile	Arg	G1n	Gln	His	Glu	Met [.]	Cys	Leu	Asn	
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cac	tca	aac	caa	ttc	acc	cag	ctg	ggc	aac	atc	act	gaa	acc	acc	aag	2065
His	Ser	Asn	Gln	Phe	Thr	G1n	Leu	Gly	Asn	Ile	Thr	Glu	Thr	Thr	Lys	
		595					600					605				
ttt	gaa	aag	ttg	gcg	gag	gac	tgt	aag	cgg	agc	atg	gac	att	ctg	aag	2113
Phe	Glu	Lys	Leu	Ala	Glu	Asp	Cys	Lys	Arg	Ser	Met	Asp	Ile	Leu	Lys	
	610					615					620					

caa	gcc	ttc	gtc	cgg	ggt	ctc	ccc	acg	ccc	acc	gcc	cgc	ttt	gag	caa	2161
Gln	Ala	Phe	Val	Arg	Gly	Leu	Pro	Thr	Pro	Thr	Ala	Arg	Phe	Glu	Gln	
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Arg	Thr	Phe	Ser	Val	Ile	Lys	Ile	Phe	Pro	Asp	Leu	Ser	Ser	Asn	Asp	
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Met	Leu	Leu	Phe	Ile	Val	Lys	Gly	Ile	Asn	Leu	Pro	Thr	Pro	Pro	Gly	
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Pro	Asn	Val	Glu	Glu	Ala	Gln	Lys	Asp	Lys	Thr	Ser	Val	Ile	Lys	Asn	
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aca	gac	tcc	cct	gag	ttc	aag	gag	cag	ttc	aaa	ctc	tgc	atc	aac	cgc	2401
Thr	Asp	Ser	Pro	Glu	Phe	Lys	G1u	G1n	Phe	Lys	Leu	Cys	Ile	Asn	Arg	
705					710					715					720	
agc	cac	cgt	ggc	ttc	cga	agg	gcc	atc	cag	acc	aag	ggc	atc	aag	ttc	2449
Ser	His	Arg	Gly	Phe	Arg	Arg	Ala	Ile	Gln	Thr	Lys	Gly	Ile	Lys	Phe	
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gaa	gtg	gtt	cac	aag	ggg	ggg	ctg			act	gac	cgg	gtg	ctg	ggg	2497
								688/	135							

Glu	Val	Val	His	Lys	Gly	Gly	Leu	Phe	Lys	Thr	Asp	Arg	Val	Leu	Gly	
			740					745					750			
aca	gcc	cag	ctg	aag	ctg	gat	gca	ctg	gag	ata	gca	tgt	gag	gtc	cgg	2545
Thr	Ala	Gln	Leu	Lys	Leu	Asp	Ala	Leu	Glu	Ile	Ala	Cys	Glu	Val	Arg	
		755					760					765				
gag	atc	ctt	gag	gtc	ctg	gat	ggt	cgc	cgg	ccc	aca	ggg	ggg	cga	ctg	2593
						Asp										
	770					775	,				780	,	,			
~~~	at a	at a	σ± ο	oʻaa	n++	000	~~ ~		a+~	000	~~~	000		++~	~~~	2641
						cgg										2641
	vaı	met	vai	Arg		Arg	G1u	PIO	Leu		нта	GIN	GIN	Leu		
785					790					795		•			800	
						ctg										2689
Thr	Thr	Thr	Glu	Arg	Trp	Leu	Val	Ile	Asp	Pro	Val	Pro	Ala	Ala	Val	
				805					810					815		
ccc	aca	cag	gtt	gct	ggg	ccc	aaa	ggg	aag	gcc	cct	cct	gtg	cct	gcc	2737
Pro	Thr	G1n	Val	Ala	Gly	Pro	Lys	Gly	Lys	Ala	Pro	Pro	Val	Pro	Ala	
			820					825					830			
cct	gca	agg	gag	tca	ggg	aac	aga	tca	gcc	cgg	ссс	ctg	cat	agc	ctc	2785
Pro	Ala	Arg	G1u	Ser	Gly	Asn	Arg	Ser	Ala	Arg	Pro	Leu	His	Ser	Leu	
		835					840					845				
agt	gtg	ctg	gcg	ttt	gac	caa	gag	cgt	ctg	gag	cgg	aag	atc	ctg	gcc	2833
						G1n										
			-		-			689/			Ŭ	-			<b>-</b>	

PCT/JP01/11389 WO 02/053737 ctc agg cag gcg cgg cgg ccg gtg ccc cca gaa gtg gcc cag cag tac Leu Arg Gln Ala Arg Arg Pro Val Pro Pro Glu Val Ala Gln Gln Tyr cag gac atc atg caa cgc agc cag tgg cag agg gca cag ctg gag cag Gln Asp Ile Met Gln Arg Ser Gln Trp Gln Arg Ala Gln Leu Glu Gln ggg ggt gtg ggc atc cga cgg gaa tac aca gcc cag ctg gag cgg cag Gly Gly Val Gly Ile Arg Arg Glu Tyr Thr Ala Gln Leu Glu Arg Gln ctg cag ttc tac acg gag gct gcc cgg cgc ctg ggc aac gat ggc agc Leu Gln Phe Tyr Thr Glu Ala Ala Arg Arg Leu Gly Asn Asp Gly Ser agg gat gct gca aag gag gcg ctc tat agg cgg aat ctg gta ggg agt Arg Asp Ala Ala Lys Glu Ala Leu Tyr Arg Arg Asn Leu Val Gly Ser 

gag ctg cag cgg ctc cgc agg tgaggagccc atgggggggg cagcccccag 3124
Glu Leu Gln Arg Leu Arg Arg
945 950

aaagcgggca gcaggccccg ataccgggaa gagccgacac agccacgaac cagacaagca 3184

gacaatcagc ggacaatcgg ttctggactc acccctcatc cgggccccca gccccgccag 3244 690/735

agecteget gegecetgga gagteetgtt tgeacageee aggggtgtee ggeetetgge 3364

cegeeeegga geagggagg eggetggge eaageeeega gggeeeetge aageaettta 3424

ctteetgtte eteeeeagee ttaaceeeaa ageeeteetg eaceeeaaag aageeaetga 3484

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<210> 172

<211> 951

<212> PRT

<213> Homo sapiens

<400> 172

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Met Ile Pro Glu Asp Gly Ala Asn Asp Glu Glu Leu Glu Ala Glu Phe
35 40 45

Leu Ala Leu Val Gly Gly Gln Pro Pro Ala Leu Glu Lys Leu Lys Gly 50 55 60 Lys Gly Pro Leu Pro Met Glu Ala Ile Glu Lys Met Ala Ser Leu Cys 65 70 75 80 Met Arg Asp Pro Asp Glu Asp Glu Glu Glu Gly Thr Asp Glu Asp Asp 85 90 95 Leu Glu Ala Asp Asp Asp Leu Leu Ala Glu Leu Asn Glu Val Leu Gly 100 105 110 Glu Glu Gln Lys Ala Ser Glu Thr Pro Pro Pro Val Ala Gln Pro Lys 115 120 125 Pro Glu Ala Pro His Pro Gly Leu Glu Thr Thr Leu Gln Glu Arg Leu

Pro Glu Ala Pro His Pro Gly Leu Glu Thr Thr Leu Gln Glu Arg Leu
130 135 140

Ala Leu Tyr Gln Thr Ala Ile Glu Ser Ala Arg Gln Ala Gly Asp Ser 145 150 155 160

Ala Lys Met Arg Arg Tyr Asp Arg Gly Leu Lys Thr Leu Glu Asn Leu
165 170 175

Leu Ala Ser Ile Arg Lys Gly Asn Ala Ile Asp Glu Ala Asp Ile Pro 180 185 190

Pro Pro Val Ala Ile Gly Lys Gly Pro Ala Ser Thr Pro Thr Tyr Ser

195
200
205
692/735

Pro	Ala	Pro	Thr	Gln	Pro	Ala	Pro	Arg	Ile	Ala	Ser	Ala	Pro	Glu	Pro
	210					215					220				
A	Vol	The	Lou	C1	C1	Dwo	Son.	410	The	Λla	Dwo	<b>11</b> 0	Com	Com.	Dwa
	Val	1111	Leu	Glu			Ser	міа	mr		FIO	ита	Ser	ser	
225					230					235					240
Gly	Leu	Ala	Lys	Pro	G1n	Met	Pro	Pro	Gly	Pro	Cys	Ser	Pro	Gly	Pro
				245					250					255	
Leu	Ala	G1n	Leu	Gln	Ser	Arg	Gln	Arg	Asp	Tyr	Lys	Leu	Ala	Ala	Leu
			260					265					270		
His	Ala	Lys	G1n	G1n	Gly	Asp	Thr	Thr	Ala	Ala	Ala	Arg	His	Phe	Arg
		275					280					285			
Val		Lys	Ser	Phe	Asp		Val	Leu	Glu	Ala		Ser	Arg	Gly	Glu
	290					295					300				
Pro	Va 1	Acn	I au	Ser	Cvc	Lou	Dro	Dro	Dwa	Dro	Aan	C1 n	Lou	Dmo	Dwa
305	141	nsp	Lcu	OCI	310	Leu	110	110	110	315	nsp	GIII	Leu	110	320
000					510					310					320
Asp	Pro	Pro	Ser	Pro	Pro	Ser	Gln	Pro	Pro	Thr	Pro	Ala	Thr	Ala	Pro
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Ser	Thr	Thr	Glu	Val	Pro	Pro	Pro	Pro	Arg	Thr	Leu	Leu	Glu	Ala	Leu
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7111	Gln	Arg	Met	Glu	Arg	Tvr	G1n	Val	Ala	Ala	Ala	G1n	Ala	Lvs	Ser

355 360 365

Lys Gly Asp Gln Arg Lys Ala Arg Met His Glu Arg Ile Val Lys Gln 370 375 380

Tyr Gln Asp Ala Ile Arg Ala His Lys Ala Gly Arg Ala Val Asp Val
385 390 395 400

Ala Glu Leu Pro Val Pro Pro Gly Phe Pro Pro Ile Gln Gly Leu Glu
405 410 415

Ala Thr Lys Pro Thr Gln Gln Ser Leu Val Gly Val Leu Glu Thr Ala
420 425 430

Met Lys Leu Ala Asn Gln Asp Glu Gly Pro Glu Asp Glu Glu Asp Glu
435 440 445

Val Pro Lys Lys Gln Asn Ser Pro Val Ala Pro Thr Ala Gln Pro Lys
450 455 460

Ala Pro Pro Ser Arg Thr Pro Gln Ser Gly Ser Ala Pro Thr Ala Lys
465 470 475 480

Ala Pro Pro Lys Ala Thr Ser Thr Arg Ala Gln Gln Gln Leu Ala Phe
485 490 495

Leu Glu Gly Arg Lys Lys Gln Leu Leu Gln Ala Ala Leu Arg Ala Lys
500 505 510

WO 02/053737	PCT/JP01/11389

G1n	Lys	Asn 515	Asp	Val	Glu	Gly	Ala 520	Lys	Met	His	Leu	Arg 525	Gln	Ala	Lys
Gly	Leu 530	G1u	Pro	Met	Leu	G1u 535	Ala	Ser	Arg	Asn	G1y 540	Leu	Pro	Val	Asp
Ile 545	Thr	Lys	Val	Pro	Pro 550	Ala	Pro	Val	Asn	Lys 555	Asp	Asp	Phe	Ala	Leu 560
Val ·	Gln	Arg	Pro	Gly 565	Pro	Gly	Leu	Ser	G1n 570	G1u	Ala	Ala	Arg	Arg 575	Tyr
Gly	Glu	Leu	Thr 580	Lys	Leu	Ile	Arg	G1n 585	Gln	His	G1u	Met	Cys 590	Leu	Asn
His	Ser	Asn 595	Gln	Phe	Thr	Gln	Leu 600	Gly	Asn	Ile	Thr	G1u 605	Thr	Thr	Lys
Phe	Glu 610	Lys	Leu	Ala	Glu	Asp 615	Cys	Lys	Arg	Ser	Met 620	Asp	Ile	Leu	Lys
Gln 625	Ala	Phe	Val	Arg	Gly 630	Leu	Pro	Thr	Pro	Thr 635	Ala	Arg	Phe	Glu	Gln 640
Arg	Thr .	Phe	Ser	Val 645	Ile	Lys	Ile		Pro 650	Asp	Leu	Ser		Asn 655	Asp
Met	Leu		Phe 660	Ile	Val	Lys		Ile 665 <b>69</b> 5/′		Leu	Pro		Pro 670	Pro	Gly

Leu	Ser	Pro 675	Gly	Asp	Leu	Asp	Val 680	Phe	Val	Arg	Phe	Asp 685	Phe	Pro	Tyr
Pro	Asn 690		Glu	Glu	Ala	Gln 695		Asp	Lys	Thr	Ser 700		Ile	Lys	Asn
Thr 705		Ser	Pro	Glu	Phe 710		Glu	Gln	Phe	Lys 715		Cys	Ile	Asn	Arg 720
Ser	His	Arg	Gly	Phe 725	Arg	Arg	Ala	Ile	G1n 730	Thr	Lys	Gly	Ile	Lys 735	Phe
Glu	Val	Val	His 740	Lys	Gly	Gly	Leu	Phe 745	Lys	Thr	Asp	Arg	Val 750	Leu	Gly
Γhr	Ala	G1n 755	Leu	Lys	Leu	Asp	Ala 760	Leu	Glu	Ile	Ala	Cys 765	Glu	Val	Arg
Glu	Ile 770	Leu	Glu	Val	Leu	Asp 775	Gly	Arg	Arg	Pro	Thr 780	Gly	Gly	Arg	Leu
31u 785	Val	Met	Val	Arg	Ile 790	Arg	Glu	Pro	Leu	Thr 795	Ala	Gln	Gln	Leu	G1u 800
ſhr	Thr	Thr	Glu	Arg 805	Trp	Leu	Val	Ile	Asp 810	Pro	Val	Pro	Ala	Ala 815	Val

Pro Thr Gln Val Ala Gly Pro Lys Gly Lys Ala Pro Pro Val Pro Ala

820 825 830

Pro Ala Arg Glu Ser Gly Asn Arg Ser Ala Arg Pro Leu His Ser Leu 835 840 845

Ser Val Leu Ala Phe Asp Gln Glu Arg Leu Glu Arg Lys Ile Leu Ala 850 855 860

Leu Arg Gln Ala Arg Arg Pro Val Pro Pro Glu Val Ala Gln Gln Tyr 865 870 875 880

Gln Asp Ile Met Gln Arg Ser Gln Trp Gln Arg Ala Gln Leu Glu Gln 885 890 895

Gly Gly Val Gly Ile Arg Arg Glu Tyr Thr Ala Gln Leu Glu Arg Gln 900 905 910

Leu Gln Phe Tyr Thr Glu Ala Ala Arg Arg Leu Gly Asn Asp Gly Ser 915 920 925

Arg Asp Ala Ala Lys Glu Ala Leu Tyr Arg Arg Asn Leu Val Gly Ser 930 935 940

Glu Leu Gln Arg Leu Arg Arg 945 950

<210> 173

<211> 2796

<212> DNA

<213> Mus musculus

<220>

<221> CDS

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<400> 173

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1 5

gac	ttc	caa	ttc	caa	gat	tta	aat	tca	agt	ctc	aga	ccc	agg	ttg	gga	642
Asp	Phe	Gln	Phe	Gln	Asp	Leu	Asn	Ser	Ser	Leu	Arg	Pro	Arg	Leu	Gly	
		10					15					20				
aat	gca	act	gcc	aat	aat	act	tgc	att	gtt	gat	gat	tcc	ttc	aag	tat	690
Asn	Ala	Thr	Ala	Asn	Asn	Thr	Cys	Ile	Val	Asp	Asp	Ser	Phe	Lys	Tyr	
	25					30					35					
aat	ttg	aat	ggt	gct	gtc	tat	agt	gtt	gta	ttc	atc	ctg	ggt	cta	ata	738
Asn	Leu	Asn	Gly	Ala	Val	Tyr	Ser	Val	Val	Phe	Ile	Leu	G1y	Leu	Ile	
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acc	aac	agt	gcc	tcc	ctg	ttt	gtc	ttc	tgc	ttc	cgc	atg	aaa	atg	aga	786
Thr	Asn	Ser	Ala	Ser	Leu	Phe	Val	Phe	Cys	Phe	Arg	Met	Lys	Met	Arg	
				60					65					70		
agt	gag	acg	gct	act	ttc	atc	acc	aac	ctg	gcc	ctc	tct	gat	ttg	ctt	834
Ser	Glu	Thr	Ala	Thr	Phe	Ile	Thr	Asn	Leu	Ala	Leu	Ser	Asp	Leu	Leu	
			75					80					85			
ttt	gtt	tgt	acc	cta	cct	ttc	aaa	ata	ttt	tac	aac	ttt	aat	cgc	cac	882
Phe	Val	Cys	Thr	Leu	Pro	Phe	Lys	Ile	Phe	Tyr	Asn	Phe	Asn	Arg	His	
		90					95					100				
tgg	cct	ttt	ggt	gac	acc	ctc	tgt	aag	atc	tca	ggg	act	gcg	ttc	ctc	930
_	_						_	_		Ser						

110

699/735

115

105

acc	aac	atc	tat	ggg	agc	atg	ctc	ttc	ctc	acc	tgc	atc	agt	gtg	gat	978
Thr	Asn	Ile	Tyr	Gly	Ser	Met	Leu	Phe	Leu	Thr	Cys	Ile	Ser	Val	Asp	
120					125					130					135	
cgt	ttc	cta	gcc	att	gtc	tat	ccc	ttc	cga	tcg	cgt	acc	atc	agg	acc	1026
Arg	Phe	Leu	Ala	Ile	Val	Tyr	Pro	Phe	Arg	Ser	Arg	Thr	Ile	Arg	Thr	
				140					145					150		
agg	agg	aat	tcc	gcc	att	gtg	tgc	gct	gga	gtc	tgg	atc	cta	gtc	ctc	1074
Arg	Arg	Asn	Ser	Ala	Ile	Val	Cys	Ala	Gly	Val	Trp	Ile	Leu	Val	Leu	
			155					160					165			
agt	ggt	ggt	att	tca	gct	tct	ttg	ttc	tcc	acc	act	aat	gtc	aac	aat	1122
Ser	Gly	Gly	Ile	Ser	Ala	Ser	Leu	Phe	Ser	Thr	Thr	Asn	Val	Asn	Asn	
		170					175					180				
gcg	acc	acc	act	tgc	ttt	gaa	ggc	ttc	tcc	aaa	cgt	gtc	tgg	aag	aca	1170
Ala	Thr	Thr	Thr	Cys	Phe	Glu	Gly	Phe	Ser	Lys	Arg	Val	Trp	Lys	Thr	
	185					190					195					
tac	ctg	tcc	aag	atc	act	ata	ttc	att	gaa	gtt	gtt	gga	ttc	atc	att	1218
Tyr	Leu	Ser	Lys	Ile	Thr	Ile	Phe	Ile	Glu	Val	Val	Gly	Phe	Ile	Ile	
200					205					210					215	
cct	ctg	ata	ttg	aat	gtt	tct	tgt	tct	tct	gtg	gtg	ctt	aga	acc	ctc	1266
Pro													_			
				220			•		225				-3	230		

cgc	aag	cct	gca	aca	ttg	tct	cag	att	ggg	acc	aat	aag	aaa	aaa	gtg	1314
Arg	Lys	Pro	Ala	Thr	Leu	Ser	Gln	Ile	Gly	Thr	Asn	Lys	Lys	Lys	Val	
			235					240					245			
ttg	aag	atg	atc	aca	gtg	cat	atg	gca	gtg	ttt	gtg	gta	tgc	ttt	gta	1362
Leu	Lys	Met	Ile	Thr	Val	His	Met	Ala	Val	Phe	Val	Val	Cys	Phe	Val	
		250					255					260				
cca	tac	aac	tcc	gtt	ctc	ttt	tta	tat	gcc	ttg	gta	cgc	tcc	caa	gcc	1410
Pro	Tyr	Asn	Ser	Val	Leu	Phe	Leu	Tyr	Ala	Leu	Val	Arg	Ser	Gln	Ala	
	265					270					275					
att	act	aat	tgc	tta	ttg	gaa	agg	ttt	gca	aag	atc	atg	tac	cca	att	1458
Ile	Thr	Asn	Cys	Leu	Leu	Glu	Arg	Phe	Ala	Lys	Ile	Met	Tyr	Pro	Ile	
280					285					290					295	
acc	ttg	tgc	ctt	gca	act	ctg	aat	tgt	tgc	ttt	gat	cct	ttt	atc	tat	1506
Thr	Leu	Cys	Leu	Ala	Thr	Leu	Asn	Cys	Cys	Phe	Asp	Pro	Phe	Ile	Tyr	
				300					305					310		
tac	ttc	act	ctt	gaa	tcc	ttt	cag	aag	tcc	ttt	tat	atc	aat	aca	cat	1554
Гуr	Phe	Thr	Leu	Glu	Ser	Phe	G1n	Lys	Ser	Phe	Tyr	Ile	Asn	Thr	His	
			315					320					325			
ata	agg	atg	gag	tcg	ctg	ttt	aag	act	gag	aca	cct	ctg	acc	ccc	aaa -	1602
lle	Arg	Met	G1u	Ser	Leu	Phe	Lys	Thr	G1u	Thr	Pro	Leu	Thr	Pro	Lys	
		330					335					340				
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aat ggt ggt gaa tta atg ctg gaa tcc acc ttc taggtaccag aattgtcttt 1703 Asn Gly Gly Glu Leu Met Leu Glu Ser Thr Phe 360 365 370

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<212> PRT

<213> Mus musculus

<400> 174

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Cys	Phe	Arg	Met	Lys	Met	Arg	Ser	Glu	Thr	Ala	Thr	Phe	Ile	Thr	Asn
65					70					75					80
Leu	Ala	Leu	Ser	Asp	Leu	Leu	Phe	Val	Cys	Thr	Leu	Pro	Phe	Lys	Ile
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Phe	Tyr	Asn	Phe	Asn	Arg	His	Trp	Pro	Phe	Gly	Asp	Thr	Leu	Cys	Lys
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Ile	Ser	Gly	Thr	Ala	Phe	Leu	Thr	Asn	Ile	Tyr	Gly	Ser	Met	Leu	Phe
		115					120					125			
Leu	Thr	Cys	Ile	Ser	Val	Asp	Arg	Phe	Leu	Ala	Ile	Val	Tyr	Pro	Phe
	130					135					140				
Arg	Ser	Arg	Thr	Ile	Arg	Thr	Arg	Arg	Asn	Ser	Ala	Ile	Val	Cys	Ala
145					150					155					160
Gly	Val	Trp	Ile	Leu	Val	Leu	Ser	Gly	G1y	Ile	Ser	Ala	Ser	Leu	Phe
-		•		165				•	170		-			175	
Ser '	Thr	Thr	Aen	Val	Asn	Asn	Ala	ፐbኍ	Th≠	Thr	Cve	Pho	G1::	G1 v	Phe
			41011	1 44.4	*****					4 4 4 4	~, ~	* *1C		- L J	4 410

185

704/735

190

180

Ser	Lys		Val	Trp	Lys	Thr	Tyr	Leu	Ser	Lys	Ile	Thr	Ile	Phe	Ile
		195					200					205			
Glu		Val	Gly	Phe	Ile			Leu	Ile	Leu	Asn	Val	Ser	Cys	Ser
	210					215					220				
	Val	Val	Leu	Arg		Leu	Arg	Lys	Pro		Thr	Leu	Ser	Gln	Ile
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Gly	Thr	Asn	Lys		Lys	Val	Leu	Lys		Ile	Thr	Val	His		Ala
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Val	Phe	Val		Cys	Phe	Val	Pro		Asn	Ser	Val	Leu		Leu	Tyr
			260					265					270		
Ala	Leu		Arg	Ser	Gln	Ala		Thr	Asn	Cys	Leu		Glu	Arg	Phe
		275					280					285			
Ala		Ile	Met	Tyr	Pro		Thr	Leu	Cys	Leu	Ala	Thr	Leu	Asn	Cys
	290					295					300				
	Phe	Asp	Pro	Phe		Tyr	Tyr	Phe	Thr		Glu	Ser	Phe	Gln	
305					310					315					320
Ser	Phe	Tyr	Ile		Thr	His	Ile	Arg		Glu	Ser	Leu	Phe		Thr
				325					330					335	
lu	Thr	Pro	Leu	Thr	Pro	Lys	Pro	Ser	Leu	Pro	Ala	Ile	Gln	Glu	Glu

340 345 350

Val Ser Asp Gln Thr Thr Asn Asn Gly Gly Glu Leu Met Leu Glu Ser

355 360 365

Thr Phe

370

<210> 175

<211> 2299

<212> DNA

<213> Homo sapiens

<220>

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<222> (67).. (1176)

<400> 175

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Met Gly Asp Arg Arg Phe Ile Asp Phe Gln Phe Gln Asp Ser

1 5 10

aat toa ago oto aga ooo agg ttg ggo aat got act goo aat aat act 156 Asn Ser Ser Leu Arg Pro Arg Leu Gly Asn Ala Thr Ala Asn Asn Thr

15 20 25 30

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Cys	Ile	Val	Asp	Asp	Ser	Phe	Lys	Tyr	Asn	Leu	Asn	Gly	Ala	Val	Tyr	
				35					40					45		
							•									
agt	gtt	gta	ttc	atc	ttg	ggt	ctg	ata	acc	aac	agt	gtc	tct	ctg	ttt	252
Ser	· Val	Val	Phe	Ile	Leu	Gly	Leu	Ile	Thr	Asn	Ser	Va1	Ser	Leu	Phe	
			50					55					60			
gto	ttc	tgt	ttc	cgc	atg	aaa	atg	aga	agt	gag	act	gct	att	ttt	atc	300
Val	Phe	Cys	Phe	Arg	Met	Lys	Met	Arg	Ser	Glu	Thr	Ala	Ile	Phe	Ile	
		65					70					75				
	aat								•							348
Thr	Asn	Leu	Ala	Val	Ser		Leu	Leu	Phe	Val		Thr	Leu	Pro	Phe	
	80					85					90					
	_ + _	4.4.4.														000
	ata															396
	Ile	Pne	ıyr	ASN		Asn	Arg	нıs	irp		Pne	GIY	Asp	inr		
95					100					105					110	
+ 00	000	a+a	+ 0 +	~~~	20+	<b>700</b>	++0	a++			a+a	+-+	~~~			444
	aag															444
Cys	Lys	116	per	115	1111	ліа	rne	Leu	120	ASII	116	1 )1	СТУ		Mer	
				110					120					125		
cto	ttt	cto	200	+a+	att	aat	ata	na+	o a t	++0	ct a	acc	2++	ata	+++	402
	Phe															492
Leu	1 116	Leu	130	Oy 3	116	Jei	, a1	135	urg	1 116	Den	ura	140	va1	1 AT	
			100					100					140			

cct	ttt	cga	tct	cgt	act	att	agg	act	agg	agg	aat	tct	gcc	att	gtg	540
Pro	Phe	Arg	Ser	Arg	Thr	Ile	Arg	Thr	Arg	Arg	Asn	Ser	Ala	Ile	Val	
		145					150					155				
tgt	gct	ggt	gtc	tgg	atc	cta	gtc	ctc	agt	ggc	ggt	att	tca	gcc	tct	588
Cys	Ala	Gly	Val	Trp	Ile	Leu	Val	Leu	Ser	G1y	Gly	Ile	Ser	Ala	Ser	
	160					165					170					
ttg	ttt	tcc	acc	act	aat	gtc	aac	aat	gca	acc	acc	acc	tgc	ttt	gaa	636
Leu	Phe	Ser	Thr	Thr	Asn	Val	Asn	Asn	Ala	Thr	Thr	Thr	Cys	Phe	Glu	
175					180					185					190	
ggc	ttc	tcc	aaa	cgt	gtc	tgg	aag	act	tat	tta	tcc	aag	atc	aca	ata	684
Gly	Phe	Ser	Lys	Arg	Val	Trp	Lys	Thr	Tyr	Leu	Ser	Lys	Ile	Thr	Ile	
				195					200					205		
		gaa												_		732
Phe	Ile	G1u		Val	Gly	Phe	Ile		Pro	Leu	Ile	Leu	Asn	Val	Ser	
			210					215					220			
<b>.</b> .			,				•									===
		tct														780
Lys	Ser	Ser	Val	Val	Leu	Arg		Leu	Arg	Lys	Pro		Thr	Leu	Ser	
		225					230					235				
	2++	aaa	200	22+	000	000	222	at a	ot a	222	0+0	a+ a		~+~	aa+	000
		ggg Gly												-		828
J.11	240	O.L.y	1111	non	Lys	245	БуЗ	vai	Leu	<b>D</b> , 3	250	116	1111	vai	1113	
	210					<b>41</b> 0					200					
atø	gea	gtc	ttt	øt.ø	gta	tgc	ttt	pts	ccc	tac	aac	tet	ato	ctc	tte	876
~~8	avu	200	500	0.0	- Ju	250		709/		540		300	800		300	υų

Met Ala Val Phe Val Val Cys Phe Val Pro Tyr Asn Ser Val Leu Phe

255					260					265					270	
ttg	tat	gcc	ctg	gtg	cgc	tcc	caa	gct	att	act	aat	tgc	ttt	ttg	gaa	924
Leu	Tyr	Ala	Leu	Val	Arg	Ser	Gln	Ala	Ile	Thr	Asn	Cys	Phe	Leu	G1u	
				275					280					285		
aga	ttt	gca	aag	atc	atg	tac	cca	atc	acc	ttg	tgc	ctt	gca	act	ctg	972
Arg	Phe	Ala	Lys	Ile	Met	Tyr	Pro	Ile	Thr	Leu	Cys	Leu	Ala	Thr	Leu	
			290					295					300			
aac	tgt	tgt	ttt	gac	cct	ttc	atc	tat	tac	ttc	acc	ctt	gaa	tcc	ttt	1020
Asn	Cys	Cys	Phe	Asp	Pro	Phe	Ile	Tyr	Tyr	Phe	Thr	Leu	Glu	Ser	Phe	
		305					310					315				
cag	aag	tcc	ttc	tac	atc	aat	gcc	cac	atc	aga	atg	gag	tcc	ctg	ttt	1068
Gln	Lys	Ser	Phe	Tyr	.Ile	Asn	A1a	His	Ile	Arg	Met	G1u	Ser	Leu	Phe	
	320					325					330					
aag	act	gaa	aca	cct	ttg	acc	aca	aag	cct	tcc	ctt	cca	gct	att	caa	1116
Lys	Thr	Glu	Thr	Pro	Leu	Thr	Thr	Lys	Pro	Ser	Leu	Pro	Ala	Ile	Gln	
335					340					345					350	
gag	gaa	gtg	agt	gat	caa	aca	aca	aat	aat	ggt	ggt	gaa	tta	atg	cta	1164
Glu	G1u	Val	Ser	Asp	Gln	Thr	Thr	Asn	Asn	G1y	Gly	Glu	Leu	Met	Leu	
				355					360					365		
gaa	tcc	acc	ttt	tage	tate	ag a	aate	tgtt	c ag	gtco	agat	atg	gttt	ctc		1216
Glu	Ser	Thr	Phe													
								709/	735							

370

ctataatttt teetatgeta taaactaaag atttgaaget aatgataetg agaataatge 1276 accaaatcca gtcagataca tttgtttgaa ggtatactgt agagttttta ttgctgtttt 1336 gttcagtaat tataggtcaa atctaattac aacaaccaag atggattgcc aaactcttct 1396 gcttggttgg aatttcattg tatcgcatta tccaggtggc tagtggcatt tgataatata 1456 gagatgactt tgaaactttc aaaaaggtat ttctattcca atgatatttg gtaattaggt 1516 tgggcctata aatatagaac aaattcaggg atttttaaaa aattgtgtta ctactgatat 1576 atgctagttt tattttattt ttttggactg tcattgagtt tattttagca caagaatatt 1636 tttagcctaa cattattaat aagaaatgtg tcaaattttt aacattggta aaatatgtta 1696 tgtgcatttt gaaaacagaa aacaaattgc gttggcatgt acgtgggtgg gaagaaaaag 1756 aaaattaaca ggatttacac aattataatc accagcagtg tgagtttaaa aaacttcgtt 1816 gtttttacac caaattaaaa ttttcatgtc aaacttcaaa gccagaaagc tgctaaatac 1876 gtgtctggca ggtaaaagct ggaaaattac ttaaaacagg aaagtgtcaa taaaaaaact 1936 tgagcaacac caacatattt tttcttaaaa tgtcacgtta tcttcatttt gggaaactag 1996 710/735

<210> 176

<211> 370

<212> PRT

<213> Homo sapiens

<400> 176

Met Gly Asp Arg Arg Phe Ile Asp Phe Gln Phe Gln Asp Ser Asn Ser

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Ser Leu Arg Pro Arg Leu Gly Asn Ala Thr Ala Asn Asn Thr Cys Ile
20 25 30

Val Asp Asp Ser Phe Lys Tyr Asn Leu Asn Gly Ala Val Tyr Ser Val
35 40 45

Val Phe Ile Leu Gly Leu Ile Thr Asn Ser Val Ser Leu Phe Val Phe
50 55 60
711/735

Cys	Phe	Arg	Met	Lys	Met	Arg	Ser	Glu	Thr	Ala	Ile	Phe	Ile	Thr	Asn
65					70					75					80
Leu	Ala	Val	Ser	Asp 85	Leu	Leu	Phe	Val	Cys 90	Thr	Leu	Pro	Phe	Lys 95	Ile
Phe	Tyr	Asn	Phe 100	Asn	Arg	His	Trp	Pro 105	Phe	Gly	Asp	Thr	Leu 110	Cys	Lys
Ile	Ser	Gly 115	Thr	Ala	Phe	Leu	Thr 120	Asn	Ile	Tyr	Gly	Ser 125	Met	Leu	Phe
Leu	Thr 130	Cys	Ile	Ser	Val	Asp 135	Arg	Phe	Leu	Ala	Ile 140	Val	Tyr	Pro	Phe
Arg 145	Ser	Arg	Thr	Ile	Arg 150	Thr	Arg	Arg	Asn	Ser 155	Ala	Ile	Val	Cys	Ala 160
Gly	Val	Trp	Ile	Leu 165	Val	Leu	Ser	Gly	Gly 170	Ile	Ser	Ala	Ser	Leu 175	Phe
Ser	Thr	Thr	Asn 180	Val	Asn	Asn	Ala	Thr 185	Thr	Thr	Cys	Phe	Glu 190	Gly	Phe
Ser		Arg 195	Val	Trp	Lys		Tyr 200	Leu	Ser	Lys		Thr 205	Ile	Phe	Ile
Glu	Val	Val	G1y	Phe	Ile	Ile	Pro	Leu 712/		Leu	Asn	Val	Ser	Cys	Ser

210 215 220

Ser Val Val Leu Arg Thr Leu Arg Lys Pro Ala Thr Leu Ser Gln Ile 225 230 235 240

Gly Thr Asn Lys Lys Val Leu Lys Met Ile Thr Val His Met Ala 245 250 255

Val Phe Val Val Cys Phe Val Pro Tyr Asn Ser Val Leu Phe Leu Tyr 260 265 270

Ala Leu Val Arg Ser Gln Ala IIe Thr Asn Cys Phe Leu Glu Arg Phe
275 280 285

Ala Lys Ile Met Tyr Pro Ile Thr Leu Cys Leu Ala Thr Leu Asn Cys 290 295 300

Cys Phe Asp Pro Phe Ile Tyr Tyr Phe Thr Leu Glu Ser Phe Gln Lys 305 310 315 320

Ser Phe Tyr Ile Asn Ala His Ile Arg Met Glu Ser Leu Phe Lys Thr 325 330 335

Glu Thr Pro Leu Thr Thr Lys Pro Ser Leu Pro Ala Ile Gln Glu Glu
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Val Ser Asp Gln Thr Thr Asn Asn Gly Gly Glu Leu Met Leu Glu Ser 355 360 365

Thr Phe

370

<210> 177

<211> 973

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (30).. (416)

<400> 177

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Met Ala Arg Gly Ser Leu Arg Arg

1 5

gtg gcc ggg gag caa gcg cca ggc acc gcc ccc tgc tcc cgc ggc agc 149
Val Ala Gly Glu Gln Ala Pro Gly Thr Ala Pro Cys Ser Arg Gly Ser
25 30 35 40

tcc tgg agc gcg gac ctg gac aag tgc atg gac tgc gcg tct tgc agg 197 Ser Trp Ser Ala Asp Leu Asp Lys Cys Met Asp Cys Ala Ser Cys Arg 714/735

WO 02/053737			PCT/JP01/11389
	45	50	55

gcg cga ccg cac agc gac ttc tgc ctg ggc tgc gct gca gca cct cct 245
Ala Arg Pro His Ser Asp Phe Cys Leu Gly Cys Ala Ala Ala Pro Pro
60 65 70

gcc ccc ttc cgg ctg ctt tgg ccc atc ctt ggg ggc gct ctg agc ctg 293
Ala Pro Phe Arg Leu Leu Trp Pro Ile Leu Gly Gly Ala Leu Ser Leu
75 80 85

acc ttc gtg ctg ggg ctg ctt tct ggc ttt ttg gtc tgg aga cga tgc 341

Thr Phe Val Leu Gly Leu Leu Ser Gly Phe Leu Val Trp Arg Arg Cys
90 95 100

cgc agg aga gag aag ttc acc acc ccc ata gag gag acc ggc gga gag 389
Arg Arg Arg Glu Lys Phe Thr Thr Pro IIe Glu Glu Thr Gly Gly Glu
105 110 115 120

ggc tgc cca gct gtg gcg ctg atc cag tgacaatgtg ccccctgcca 436
Gly Cys Pro Ala Val Ala Leu Ile Gln

125

geeggggete geecacteat catteattea tecattetag ageeagtete tgeeteecag 496
acgeggeggg ageeaagete etecaaceae aaggggggtg gggggeggtg aateacetee 556
gaggeetggg tecagggtte aggggaacet tecaaggtgt etggttgeee tgeetetgge 616
tecagaacag aaagggagee teacgetgge teacacaaaa cagetgacae tgactaagga 676
715/735

actgcagcat ttgcacaggg gaggggggtg ccctccttcc tagaggccct gggggccagg 736
ctgacttggg gggcagactt gacactaggc cccactcact cagatgtcct gaaattccac 796
cacgggggtc accctggggg gttagggacc tattttaac actagggggc tggcccacta 856
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<210> 178

<211> 129

<212> PRT

<213> Homo sapiens

<400> 178

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1 5 10 15

Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly
20 25 30

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys
35 40 45

Cys Met Asp Cys Ala Ser Cys Arg Ala Arg Pro His Ser Asp Phe Cys
50 55 60
716/735

Leu Gly Cys Ala Ala Ala Pro Pro Ala Pro Phe Arg Leu Leu Trp Pro

65 70 75 80

Ile Leu Gly Gly Ala Leu Ser Leu Thr Phe Val Leu Gly Leu Leu Ser

85 90 95

Gly Phe Leu Val Trp Arg Arg Cys Arg Arg Arg Glu Lys Phe Thr Thr
100 105 110

Pro Ile Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu Ile 115 120 125

Gln

<210> 179

⟨211⟩ 3631

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (191).. (3244)

<400> 179

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WO 02/053737	PCT/JP01/11389

ggc	gctg	gcg	caag	gatga	atg t	tgct	ccat	a tt	ttaa	aacg	gag	ccag	gcc	tacc	acagat	120
cca	cctg	gaa	ggga	acce	gcc t	tgtt	ctca	c ct	gcct	tgcc	gaa	ggga	gct	ggcc	tttgga	180
gtt	caag	tgg	atg	cgc	gat	gac	agt	gag	ctc	acc	acc	tac	agc	agc	gaa	229
			Met	Arg	Asp	Asp	Ser	Glu	Leu	Thr	Thr	Tyr	Ser	Ser	Glu	
			1				5					10				
tat	aag	tac	att	att	cca	tct	ttg	cag	aag	ctc	gat	gct	ggg	ttt	tac	277
Tyr	Lys	Tyr	· Ile	· Ile	Pro	Ser	Leu	G1n	Lys	Leu	Asp	Ala	Gly	Phe	Tyr	
	15					20					25					
cgc	tgc	gtg	gtg	cga	aac	aga	atg	gga	gca	ctc	ctg	caa	aga	aaa	tca	325
Arg	Cys	Val	Val	Arg	Asn	Arg	Met	Gly	Ala	Leu	Leu	Gln	Arg	Lys	Ser	
30					35					40					45	
gaa	gtt	caa	gtc	gca	tat	atg	gga	agt	ttc	atg	gat	acg	gac	cag	agg	373
Glu	Val	Gln	Val	Ala	Tyr	Met	Gly	Ser	Phe	Met	Asp	Thr	Asp	G1n	Arg	
				50					55					60		
aaa	aca	gtt	tct	caa	gga	cgt	gca	gcg	att	cta	aac	ctg	ctg	ccc	atc	421
Lys	Thr	Val	Ser	G1n	Gly	Arg	Ala	Ala	Ile	Leu	Asn	Leu	Leu	Pro	Ile	
			65					70					75			
acc	agc	tac	ccc	aga	cct	caa	gtg	act	tgg	ttt	aga	gaa	ggg	cac	aag	469
Thr	Ser			Arg	Pro	G1n	Val	Thr	Trp	Phe	Arg	.Glu	Gly	His	Lys	
		80					85 ·					90				
att	att	cca	agc	aac	aga	ata	gcc	atc 718/		ttg	gag	aat	cag	ctg	gtg	517

Ile	Ile	Pro	Ser	Asn	Arg	Ile	Ala	Ile	Thr	Leu	Glu	Asn	Gln	Leu	Val	
	95					100					105					
atc	ctc	gcc	acc	aca	acc	agt	gat	gcc	ggg	gca	tac	tac	gtg	cag	gcc	565
Ile	Leu	Ala	Thr	Thr	Thr	Ser	Asp	Ala	Gly	Ala	Tyr	Tyr	Val	Gln	Ala	
110					115					120					125	
gtg	aat	gag	aaa	aat	gga	gaa	aac	aag	aca	agc	cca	ttc	att	cat	ttg	613
Val	Asn	Glu	Lys	Asn	Gly	Glu	Asn	Lys	Thr	Ser	Pro	Phe	Ile	His	Leu	
				130					135					140		
agc	ata	gca	aga	gat	gtt	ggc	aca	cct	gaa	acc	atg	gcc	cca	acc	att	661
Ser	Ile	Ala	Arg	Asp	Val	Gly	Thr	Pro	G1u	Thr	Met	Ala	Pro	Thr	Ile	
			145					150					155			
gtg	gtt	ccc	ccg	ggc	aac	aga	agt	gtg	gtg	gct	gga	tcc	agt	gag	acc	709
Val	Val	Pro	Pro	Gly	Asn	Arg	Ser	Val	Val	Ala	Gly	Ser	Ser	Glu	Thr	
		160					165					170				
acc	ttg	gaa	tgt	ata	gcc	agt	gcc	agg	cct	gtg	gag	gac	ctg	agt	gtg	757
Thr	Leu	Glu	Cys	Ile	Ala	Ser	Ala	Arg	Pro	Val	Glu	Asp	Leu	Ser	Val	
	175					180					185					
acc	tgg	aag	agg	aat	gga	gtg	aga	atc	acc	agt	ggc	ctc	cac	agc	ttt	805
Thr	Trp	Lys	Arg	Asn	Gly	Val	Arg	Ile	Thr	Ser	Gly	Leu	His	Ser	Phe	
190					195					200					205	
gga	aga	cgc	ctc	acc	atc	agc	aac	ccg	acg	tcc	gcg	gac	acc	ggg	cca	853
G1y	Arg	Arg	Leu	Thr	Ile	Ser	Asn	Pro	Thr	Ser	Ala	Asp	Thr	Gly	Pro	
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210 215 220

tac gtc tgc gag gcg gcg ctg ccg ggg agc gct ttt gaa ccg gcc agg 901
Tyr Val Cys Glu Ala Ala Leu Pro Gly Ser Ala Phe Glu Pro Ala Arg
225 230 235

gcg acg gcc ttt ctt ttc atc ata gag cca cca tat ttt act gct gag 949
Ala Thr Ala Phe Leu Phe Ile Ile Glu Pro Pro Tyr Phe Thr Ala Glu
240 245 250

ccc gag agt cgg att tca gct gaa gta gaa gaa act gtg gac atc gga 997
Pro Glu Ser Arg Ile Ser Ala Glu Val Glu Glu Thr Val Asp Ile Gly
255 260 265

tgt caa gcc atg ggg gtc ccc ctt ccc acc ctc cag tgg tac aag gat 1045 Cys Gln Ala Met Gly Val Pro Leu Pro Thr Leu Gln Trp Tyr Lys Asp 270 275 280 285

gcc atc tcc atc agc agg ctc cag aat cct cga tac aaa gtg ctc gcc 1093
Ala Ile Ser Ile Ser Arg Leu Gln Asn Pro Arg Tyr Lys Val Leu Ala
290 295 300

agc gga ggc ctg cgc atc cag aag ctg cgt cca gag gac tcc gga atc 1141 Ser Gly Gly Leu Arg Ile Gln Lys Leu Arg Pro Glu Asp Ser Gly Ile 305 310 315

ttc cag tgc ttc gcc agc aat gaa gga ggg gag atc cag acc cac acc 1189

Phe Gln Cys Phe Ala Ser Asn Glu Gly Gly Glu Ile Gln Thr His Thr

320 325 330

tac	ctg	gat	gta	acc	aat	atc	gct	cca	gtg	ttc	acc	cag	cgg	cca	gtg	1237
Tyr	Leu	Asp	Val	Thr	Asn	Ile	Ala	Pro	Val	Phe	Thr	Gln	Arg	Pro	Val	
	335					340					345					
gac	acc	aca	gtt	act	gac	ggg	atg	aca	gcc	att	cta	agg	tgt	gag	gtg	1285
Asp	Thr	Thr	Val	Thr	Asp	Gly	Met	Thr	Ala	Ile	Leu	Arg	Cys	Glu	Val	
350					355					360					365	
				•												
tcc	ggg	gct	ccc	aaa	ccc	gcc	atc	acc	tgg	aaa	aga	gaa	aac	cac	att	1333
Ser	Gly	Ala	Pro	Lys	Pro	Ala	Ile	Thr	Trp	Lys	Arg	Glu	Asn	His	Ile	
				370					375					380		
ctg	gcc	agt	ggc	tct	gtc	cgg	att	cct	agg	ttc	atg	ctt	ctt	gaa	tcg	1381
Leu	Ala	Ser	Gly	Ser	Val	Arg	Ile	Pro	Arg	Phe	Met	Leu	Leu	Glu	Ser	
			385					390					395			
ggg	ggt	cta	cag	atc	gcg	ccc	gtc	ttc	atc	cag	gat	gcc	ggc	aac	tac	1429
Gly	Gly	Leu	G1n	Ile	Ala	Pro	Val	Phe	Ile	G1n	Asp	Ala	Gly	Asn	Tyr	
		400					405					410				
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Thr	Cys	Tyr	Ala	Ala	Asn	Thr	Glu	Gly	Ser	Leu	Asn	Ala	Ser	Ala	Thr	
	415					420					425					
ctc	act	gtg	tgg	aat	cgg	acg	tcc	atc	gtc	cac	cct	cct	gag	gac	cac	1525
Leu	Thr	Val	Trp	Asn	Arg	Thr	Ser	Ile	Val	His	Pro	Pro	Glu	Asp	His	
430					435					440					445	

gtg	gtg	att	aag	ggg	acc	acg	gcc	acg	ctg	cac	tgt	ggt	gcc	aca	cat	1573
Val	Val	Ile	Lys	Gly	Thr	Thr	Ala	Thr	Leu	His	Cys	Gly	Ala	Thr	His	
				450					455					460		
gac	ccc	cgg	gtt	tca	ctc	cgc	tac	gtt	tgg	aag	aag	gac	aac	gtg	gcc	1621
Asp	Pro	Arg	Val	Ser	Leu	Arg	Tyr	Val	Trp	Lys	Lys	Asp	Asn	Val	Ala	
			465					470					475			
ctg	act	cca	tcg	agc	acg	tct	agg	atc	gtg	gtg	gag	aag	gac	ggg	tcc	1669
Leu	Thr	Pro	Ser	Ser	Thr	Ser	Arg	Ile	Val	Val	Glu	Lys	Asp	Gly	Ser	
		480					485					490				
ctt	ctc	atc	agc	cag	acg	tgg	tca	ggc	gac	atc	ggt	gac	tac	agc	tgc	1717
Leu	Leu	Ile	Ser	Gln	Thr	Trp	Ser	Gly	Asp	Ile	Gly	Asp	Tyr	Ser	Cys	
	495	,				500					505					
gag	att	gtt	tct	gaa	gga	ggg	aat	gac	tcc	agg	atg	gcc	cgg	ctg	gaa	1765
Glu	Ile	Val	Ser	Glu	Gly	Gly	Asn	Asp	Ser	Arg	Met	Ala	Arg	Leu	Glu	
510					515					520					525	
gtg	att	gaa	ctg	cct	cat	tca	cct	cag	aac	ctc	ctg	gtc	agc	cct	aat	1813
Va1	Ile	Glu	Leu	Pro	His	Ser	Pro	Gln	Asn	Leu	Leu	Val	Ser	Pro	Asn	
				530					535					540		
tct	tcc	cac	agc	cac	gcc	gtg	gtg	ctc	tct	tgg	gtc	cgg	ccc	ttt	gat	1861
Ser	Ser	His	Ser	His	Ala	Val	Val	Leu	Ser	Trp	Val	Arg	Pro	Phe	Asp	
			545					550					555			
gga	aac	agt	cct	att	ctt	tat	tac	atc	gtg	gag	ctg	tct	gaa	aac	aac	1909
								722/			-					

Gly Asn Ser Pro Ile Leu Tyr Tyr Ile Val Glu Leu Ser Glu Asn Asn tct cca tgg aag gtg cat ctg tca aac gtt ggc cct gag atg aca ggc Ser Pro Trp Lys Val His Leu Ser Asn Val Gly Pro Glu Met Thr Gly gtc acc gtg agt ggc ctg act ccg gct cgt acc tat caa ttc cgg gtg Val Thr Val Ser Gly Leu Thr Pro Ala Arg Thr Tyr Gln Phe Arg Val tgc gcg gtg aat gaa gtg ggc agg ggc cag tac agt gcc gag aca agc Cys Ala Val Asn Glu Val Gly Arg Gly Gln Tyr Ser Ala Glu Thr Ser agg ttg atg cta cct gaa gaa cca ccc agt gct ccc ccg aaa aat ata Arg Leu Met Leu Pro Glu Glu Pro Pro Ser Ala Pro Pro Lys Asn Ile gtg gcc agt ggg cgg act aat cag tcc att atg gtc cag tgg cag cca Val Ala Ser Gly Arg Thr Asn Gln Ser Ile Met Val Gln Trp Gln Pro ccc cca gaa aca gag cac aac ggg gtg ttg cgt gga tac atc ctc agg Pro Pro Glu Thr Glu His Asn Gly Val Leu Arg Gly Tyr Ile Leu Arg tac cgc ctg gct ggc ctt ccc gga gag tac cag cag cgg aac atc acc Tyr Arg Leu Ala Gly Leu Pro Gly Glu Tyr Gln Gln Arg Asn Ile Thr 723/735

agc ccg gag gtg aac tac tgc ctg gtg aca gac ctg atc atc tgg aca Ser Pro Glu Val Asn Tyr Cys Leu Val Thr Asp Leu Ile Ile Trp Thr cag tat gag ata cag gtg gcg gcg tac aac ggg gcc ggt ctg ggc gtc Gln Tyr Glu Ile Gln Val Ala Ala Tyr Asn Gly Ala Gly Leu Gly Val ttc agc agg gca gtg acc gag tac acc ttg cag gga gtg ccc acc gcg Phe Ser Arg Ala Val Thr Glu Tyr Thr Leu Gln Gly Val Pro Thr Ala ccc ccg cag aac gtg cag acg gaa gcc gtg aac tcc acc acc att cag Pro Pro Gln Asn Val Gln Thr Glu Ala Val Asn Ser Thr Thr Ile Gln ttc ctg tgg aac cct ccg cct cag cag ttt atc aat ggc atc aac cag Phe Leu Trp Asn Pro Pro Pro Gln Gln Phe Ile Asn Gly Ile Asn Gln gga tac aag ctt ctg gca tgg ccg gca gat gcc ccc gag gct gtc act Gly Tyr Lys Leu Leu Ala Trp Pro Ala Asp Ala Pro Glu Ala Val Thr gtg gtc act att gcc cca gat ttc cac gga gtc cac cat gga cac ata Val Val Thr Ile Ala Pro Asp Phe His Gly Val His His Gly His Ile 785 · 724/735

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atc	caa	ggc	ctc	tca	tct	ctc	acc	acc	tac	acc	atc	gac	gtg	gcc	gct	2917
Ile	Gln	Gly	Leu	Ser	Ser	Leu	Thr	Thr	Tyr	Thr	Ile	Asp	Va1	Ala	Ala	
	895	_				900					905					
		•														

gıg	act	gcc	grg	ggc	act	ggc	ctg	grg	act	tca	tcc	acc	att	tet	tet	2900
Val	Thr	Ala	Val	Gly	Thr	Gly	Leu	Val	Thr	Ser	Ser	Thr	Ile	Ser	Ser	
910					915					920					925	
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Asn	Ile	Ser	Pro	Arg	Ser	Ala	Thr	Leu	Gl'n	Phe	Arg	Pro	Gly	Tyr	Asp	
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Gly	Lys	Thr	Ser	Ile	Ser	Arg	Trp	Ile	Val	G1u	Gly	Gln	Met	Arg	His	
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caa	ggt	gtt	gga	tta	cct	gcc	gag	gtc	aca	cag	cca	agc	cat	gaa	gcc	3157
Gln	Gly	Val	G1y	Leu	Pro	Ala	Glu	Val	Thr	Gln	Pro	Ser	His	Glu	Ala	
	975					980					985					
gga	ttg	gag	cct	gca	aac	ctc	gga	agt	ctg	tgg	ctg	ctc	agc	ctg	gtg	3205
Gly	Leu	Glu	Pro	Ala	Asn	Leu	G1y	Ser	Leu	Trp	Leu	Leu	Ser	Leu	Val	
990					995				1	.000				1	.005	
tat	tgg	tgt	tac	agc	cag	aaa	ctt	tgg	gaa	ttc	tct	tgt	tagt	tggt	ta	3254
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<400> 180

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Val Arg Asn Arg Met Gly Ala Leu Leu Gln Arg Lys Ser Glu Val Gln
35 40 45

Val Ala Tyr Met Gly Ser Phe Met Asp Thr Asp Gln Arg Lys Thr Val
50 55 60

Ser Gln Gly Arg Ala Ala Ile Leu Asn Leu Leu Pro Ile Thr Ser Tyr 65 70 75 80

Pro Arg Pro Gln Val Thr Trp Phe Arg Glu Gly His Lys Ile Ile Pro 85 90 95

Ser Asn Arg Ile Ala Ile Thr Leu Glu Asn Gln Leu Val Ile Leu Ala 100 105 110

Thr Thr Ser Asp Ala Gly Ala Tyr Tyr Val Gln Ala Val Asn Glu 115 120 125

Lys Asn Gly Glu Asn Lys Thr Ser Pro Phe Ile His Leu Ser Ile Ala 130 135 140

Pro Gly Asn Arg Ser Val Val Ala Gly Ser Ser Glu Thr Thr Leu Glu 165 170 175

Cys Ile Ala Ser Ala Arg Pro Val Glu Asp Leu Ser Val Thr Trp Lys 180 185 190

Arg Asn Gly Val Arg Ile Thr Ser Gly Leu His Ser Phe Gly Arg Arg
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200
205
728/735

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Arg	Ile	Ser	Ala 260	Glu	Val	Glu	Glu	Thr 265	Val	Asp	Ile	G1y	Cys 270	Gln	Ala
Met	Gly	Val 275	Pro	Leu	Pro	Thr	Leu 280	Gln	Trp	Tyr	Lys	Asp 285	Ala	Ile	Ser
Ile	Ser 290	Arg	Leu	Gln	Asn	Pro 295	Arg	Tyr	Lys	Val	Leu 300	Ala	Ser	Gly	Gly
Leu 305	Arg	Ile	G1n	Lys	Leu 310	Arg	Pro	Glu	Asp	Ser 315	Gly	Ile	Phe	Gln	Cys 320
Phe	Ala	Ser	Asn	G1u 325	G1y	Gly	Glu	Ile	G1n 330	Thr	His	Thr	Tyr	Leu 335	Asp
Val	Thr	Asn	Ile 340	Ala	Pro	Val	Phe	Thr 345	Gln	Arg	Pro	Val	Asp 350	Thr	Thr
Val	Thr	Asp	G1y	Met	Thr	Ala	Ile	Leu 729/		Cys	Glu	Val	Ser	Gly	Ala

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		355					360					365			
Pro	Ľys 370	Pro	Ala	Ile	Thr	Trp 375	Lys	Arg	Glu	Asn	His 380	Ile	Leu	Ala	Ser
G1y 385	Ser	Val	Arg	Ile	Pro 390	Arg	Phe	Met	Leu	Leu 395	Glu	Ser	Gly	G1y	Leu 400
Gln	Ile	Ala	Pro	Val 405	Phe	Ile	Gln	Asp	Ala 410	Gly	Asn	Tyr	Thr	Cys 415	Tyr
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Trp Asn Arg Thr Ser Ile Val His Pro Pro Glu Asp His Val Val Ile
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Lys Gly Thr Thr Ala Thr Leu His Cys Gly Ala Thr His Asp Pro Arg 450 455 460

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Ser Gln Thr Trp Ser Gly Asp Ile Gly Asp Tyr Ser Cys Glu Ile Val
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730/735

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Ser His Ala Val Val Leu Ser Trp Val Arg Pro Phe Asp Gly Asn Ser 545 550 555 560

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Ser Gly Leu Thr Pro Ala Arg Thr Tyr Gln Phe Arg Val Cys Ala Val
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731/735

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732/735

820 825 830

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Thr Gly Tyr Gln Ile Ser Trp Glu Val Tyr Gly Arg Asn Asp Ser Arg 865 870 875 888

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Val Gly Thr Gly Leu Val Thr Ser Ser Thr Ile Ser Ser Gly Val Pro 915 920 925

Pro Asp Leu Pro Gly Ala Pro Ser Asn Leu Val Ile Ser Asn Ile Ser 930 935 940

Pro Arg Ser Ala Thr Leu Gln Phe Arg Pro Gly Tyr Asp Gly Lys Thr 945 950 955 960

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965 970 975

Gly Leu Pro Ala Glu Val Thr Gln Pro Ser His Glu Ala Gly Leu Glu 980 985 990

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<223> Description of Artificial Sequence:Primer

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<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Primer

**<400> 182** 

cgacctgcag ctcgagcaca

20

735/735

## INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP01/11389

A CLASSIFICATION OF SUBJECT MATTER (See extra sheet.)									
	to International Patent Classification (IPC) or to both na	ational classification and IPC							
B. FIELDS SEARCHED									
	Minimum documentation searched (classification system followed by classification symbols)  (See extra sheet.)								
Documentar	tion searched other than minimum documentation to the	e extent that such documents are included	in the fields searched						
Gene	lata base consulted during the international search (name bank/EMBL/EMBL/DDBJ/GeneSeq, sProt/PIR/GeneSeq, JICST(JOIS)	•	rch terms used)						
C. DOCUM	MENTS CONSIDERED TO BE RELEVANT								
Category*	Citation of document, with indication, where ap	• • •	Relevant to claim No.						
P,X	WO, 01/00824, A (Protegene 1 04 January, 2001 (04.01.01), & AU 200052499 A	Inc.),	1-11,16-18, 24-26,28-31						
x	WO, 00/11942, A (Gene Logic 09 March, 2000 (09.03.00), & AU 9957989 A	Inc.),	1-11,16-18, 24-26,28-31						
x	WO, 00/61755, A (Chiron Corp 19 October, 2000 (19.10.00), & EP 1177287 A2	o.), AU 200043381 A	1-11,16-18, 24-26,28-31						
х	WO, 00/56889, A2 (Genentech 28 September, 2000 (28.09.00) & AU 200038648 A &		1-11,16-18, 24-26,28-31						
Furthe	r documents are listed in the continuation of Box C.	See patent family annex.							
			4 694 4 4 4 4						
"A" docume considered "E" earlier of date	categories of cited documents: ent defining the general state of the art which is not to be of particular relevance document but published on or after the international filing	priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot be considered novel or cannot be considered novel or cannot be considered.							
cited to special "O" docume means	ent which may throw doubts on priority claim(s) or which is establish the publication date of another citation or other reason (as specified) ent referring to an oral disclosure, use, exhibition or other	step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art							
	ent published prior to the international filing date but later e priority date claimed	"&" document member of the same patent i	amily						
	actual completion of the international search arch, 2002 (22.03.02)	Date of mailing of the international search report 09 April, 2002 (09.04.02)							
	mailing address of the ISA/ nese Patent Office	Authorized officer							
Facsimile No	0.	Telephone No.							

Form PCT/ISA/210 (second sheet) (July 1998)

## INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP01/11389

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: 12, 20, 23  because they relate to subject matter not required to be searched by this Authority, namely:  Claims 12, 20 and 23 pertain to diagnostic methods to be practiced on the human body and methods for treatment of the human body by therapy.
2. X Claims Nos.: 19, 21, 22  because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  (See extra sheet)
3. Claims Nos.:  because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:  (see extra sheet)
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
<ol> <li>As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.</li> </ol>
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

International application No.
PCT/JP01/11389

# Continuation of A. CLASSIFICATION OF SUBJECT MATTER (International Patent Classification (IPC))

#### Continuation of B. FIELDS SEARCHED

Minimum Documentation Searched (International Patent Classification (IPC))

Int.Cl7 Cl2N15/12, C07K14/47, C07K16/18, C12N1/15, C12N1/19, C12N1/21, C12N5/10, A61K31/7088, A61K38/02, A61K39/395, A61K45/00, A61K48/00, A61P29/00, A61P35/00, A61P37/00, C12Q1/68, C12N9/00, G01N33/15, G01N33/50, G01N33/53, G01N33/577, G01N33/68

Minimum documentation searched (classification system followed by classification symbols)

Continuation of Box No. | (2) of Continuation of first sheet (1)

Concerning the "ribozyme inhibiting the activation of NF-xB by the cleavage of RNA encoding the protein as set forth in claim 7" described in claim 19, the "medicinal composition produced by the method as set forth in claim 14 as inhibiting the activation of NF-xB or activating" as described in claim 21, and the "medicinal composition as set forth in claim 21" as described in claim 22, it is completely unknown what specific compounds are involved in the scopes thereof and what are not. Thus, these claims are described in an extremely unclear manner.

Continuation of Box No. II of Continuation of first sheet (1)

In the inventions as set forth in claims 1 to 11, 16 to 18, 24 to 26 and 28 to 31, the amino acid sequences represented respectively by SEQ ID NOS:1, 3, 5, 7, 9, 11, - - - 174, 176, 178 and 180 have no chemical structure in common but exhibit a common function of encoding a protein having an effect of activating NF- $\kappa$ B.

However, document 1 (JP 11-155581 A (Okamoto Hisashi) 1999.06.15) discloses the amino acid sequence of a novel protein participating in the regulation of NF-kB signal activity, a DNA sequence encoded by the protein, a transformant having this DNA, an antibody against the above novel protein and an antisense to the DNA; document 2 (Li X, et al., Proc. Natl. Acad. Sci. U.S.A. (2000 Sep), Vol. 97, No. 19, p. 10489-10493) discloses a novel protein Act1 activating NF-kB; and document 3 (Srinvasula SM, et. al., J. Biol. Chem. (1999), Vol. 274, No. 25, p. 17946-17954) discloses a novel protein CLAP activating NF-kB. Therefore, the common matter as described above falls within the category of the prior arts and thus it is not considered that the "protein having an effect of activating NF-kB" is a special technical feature in the meaning as defined in PCT Rule 13.2.

Such being the case, 90 proteins having the amino acid sequences respectively represented by SEQ ID NOS:1, 3, 5, 7, 9, 11, - - - 174, 176, 178 and 180 are not considered as relating to a group of inventions so linked as to form a single general inventive concept but to constitute groups of inventions consisting of 90 inventions respectively relating to 90 proteins different from each other.

Concerning the "method of screening a compound with respect to the NF-KB activation inhibition activity or the promotion activity" of the inventions as set forth in claims 13 to 15, the above-described common matter "protein having an effect of activating NF-KB" falls within the category of the prior art and thus cannot be regarded as a special technical feature in the meaning as defined in PCT Rule 13.2. Thus, it cannot be considered as relating to a group of inventions so linked as to form a single general inventive concept but constitute the 91st group of inventions.

Because of having no special technical feature as described above, furthermore, claim 27 constitutes the 92nd group of inventions.

Such being the case, there is no special technical matter common to all of the claims and thus these two groups of inventions are not considered as relating to a group of inventions so linked as to form a single general inventive concept.

Accordingly, it is recognized that the following 92 groups of inventions are described in the claims:

- (1) in claims 1 to 11, 16 to 18, 24 to 26 and 28 to 31, the parts concerning SEQ ID NO:1;
- (2) in claims 1 to 11, 16 to 18, 24 to 26 and 28 to 31, the parts concerning SEQ ID NO:3;
- (3) in claims 1 to 11, 16 to 18, 24 to 26 and 28 to 31, the parts concerning SEQ ID NO:5;
- (89) in claims 1 to 11, 16 to 18, 24 to 26 and 28 to 31, the parts concerning SEQ ID NO:178;
- (90) in claims 1 to 11, 16 to 18, 24 to 26 and 28 to 31, the parts concerning SEQ ID NO:180;
- (91) in claims 13 to 15, the parts concerning the method of screening a compound with respect to the NF-kB activation inhibition activity or the promotion activity"; and
- (92) the part concerning the method of acquiring a novel full-length cDNA having the function as described in claim 27.

In claims 1 to 11, 16 to 18, 24 to 26 and 28 to 31, the parts relating to SEQ ID NO:1

国際出願番号 PCT/JP01/11389

### A. 発明の風する分野の分類(国際特許分類(IPC))

Int. Cl² Cl2N15/12, C07K14/47, C07K16/18, Cl2N1/15, Cl2N1/19, Cl2N1/21, Cl2N5/10, A61K31/7088, A61K38/02, A61K39/395, A61K45/00, A61K48/00, A61P29/00, A61P35/00, A61P37/00, Cl2Q1/68, Cl2N9/00, G01N33/15, G01N33/50, G01N33/53, G01N33/57, G01N33/68

#### B. 調査を行った分野

調査を行った最小限資料(国際特許分類(IPC))

Int. Cl¹ Cl2N15/12, C07K14/47, C07K16/18, Cl2N1/15, Cl2N1/19, Cl2N1/21, Cl2N5/10, A61K31/7088, A61K38/02, A61K39/395, A61K45/00, A61K48/00, A61P29/00, A61P35/00, A61P37/00, Cl2Q1/68, Cl2N9/00, G01N33/15, G01N33/50, G01N33/53, G01N33/577, G01N33/68

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース(データベースの名称、調査に使用した用語) Genebank/EMBL/EMBL/DDBJ/GeneSeq, SwissProt/PIR/GeneSeq, JICST (JOIS), MEDLINE (STN)

引用文献の カテゴリー*_	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
PΧ	WO 01/00824 A (PROTEGENE INC)2001.01.04 & AU 200052499 A	1-11, 16-18, 24-26, 28-31
x	WO 00/11942 A (GENE LOGIC INC) 2000.03.09 & AU 9957989 A	1-11, 16-18, 24-26, 28-31
<b>X</b>	WO 00/61755 A (CHIRON CORPORATION)2000.10.19 & EP 1177287 A2 & AU 200043381 A	1-11, 16-18, 24-26, 28-31

### X C欄の続きにも文献が列挙されている。

□ パテントファミリーに関する別紙を参照。

- * 引用文献のカテゴリー
- 「A」特に関連のある文献ではなく、一般的技術水準を示す もの
- 「E」国際出願日前の出願または特許であるが、国際出願日 以後に公表されたもの
- 「L」優先権主張に疑惑を提起する文献又は他の文献の発行 日若しくは他の特別な理由を確立するために引用する 文献 (理由を付す)
- 「O」ロ頭による開示、使用、展示等に言及する文献
- 「P」国際出願日前で、かつ優先権の主張の基礎となる出願

- の日の後に公表された文献
- 「T」国際出願日又は優先日後に公表された文献であって 出願と矛盾するものではなく、発明の原理又は理論 の理解のために引用するもの
- 「X」特に関連のある文献であって、当該文献のみで発明 の新規性又は進歩性がないと考えられるもの
- 「Y」特に関連のある文献であって、当該文献と他の1以 上の文献との、当業者にとって自明である組合せに よって進歩性がないと考えられるもの
- 「&」同一パテントファミリー文献

国際調査を完了した日 22.03.02 国際調査報告の発送日 09.04.02 国際調査機関の名称及びあて先 日本国特許庁 (ISA/JP) 特許庁審査官 (権限のある職員) (日本国特許庁 (ISA/JP) 新見 浩一 (日本国・1997) (日本国・199

国际開発機関の名称及びめて先 日本国特許庁(ISA/JP) 郵便番号100-8915 東京都千代田区霞が関三丁目4番3号

新見浩一

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# 国際調査報告

国際出頭番号 PCT/JP01/11389

<u>C(続き).</u> 引用文献の カテゴリー*	関連すると認められる文献 引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号		
х	WO 00/56889 A2 (GENENTECH INC) 2000. 09. 28 & AU 200038648 A & EP 1169442 A2	1-11, 16-18, 24-26, 28-31		
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第Ⅰ概	請求の範囲の一部の調査ができないときの意見(第1ページの2の続き)	7
	N第3項(PCT17条(2)(a))の規定により、この国際調査報告は次の理由により請求の範囲の一部について作	1
1. 🗓	請求の範囲 <u>12,20,23</u> は、この国際調査機関が調査をすることを要しない対象に係るものである。 つまり、	
	請求の範囲12, 20, 23は、人体の診断方法、ヒトの身体の治療による処置方法に該当するものである。	
2. X	請求の範囲 <u>19,21,22</u> は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、	
	請求の範囲19に記載の「・・または $7$ 記載のタンパク質をコードする $RNA$ の開裂により、 $NF-\kappa B$ の活性化を阻害するリボザイム」、請求の範囲 $21$ の「 $NF-\kappa B$ の活性化を阻害または活性化するものとして請求項 $1$ 4 に記載の方法により製造された医薬組成物」、請求の範囲 $22$ の「・・請求項 $21$ 記載の医薬組成物」については、化合物として具体的にどの化合物が包含され、どのような化合物が包含されないのかが全く不明であって、請求の範囲の記載は著しく不明確である。	
3. 🗌	請求の範囲 は、従属請求の範囲であってPCT規則6.4(a)の第2文及び第3文の規定に 従って記載されていない。	
Arr ve Am	STATE ON HALL AND WALL AND WALL AND A STATE OF THE	+
第Ⅱ欄	発明の単一性が欠如しているときの意見(第1ページの3の続き)	$\frac{1}{2}$
次に対	べるようにこの国際出願に二以上の発明があるとこの国際調査機関は認めた。	
別	J紙(特別頁参照)	
		l
	•	
1. 🗌	出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求 の範囲について作成した。	
2.	追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追 加調査手数料の納付を求めなかった。	į
3. [	出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったので、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。	
_	出願人が必要な追加調査手数料を期間内に納付しなかったので、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。 請求の範囲1-11, 16-18, 24-26, 28-31のうち、配列番号 1 に関する部分	
		١
追加關查	(手数料の異識の申立てに関する注意	
L r	] 追加調査手数料の納付と共に出願人から異魔申立てがあった。 ] 追加調査手数料の納付と共に出願人から異饞申立てがなかった。	

様式PCT/ISA/210 (第1ページの続葉(1)) (1998年7月)

請求の範囲1-11, 16-18, 24-26, 28-31に係る発明の、配列番号1, 3, 5, 7, 9, 11, ・・, 174, 176, 178または18 0のいずれかで表されるアミノ酸配列は、共通の化学構造を有するものでもなく、№ k B を活性化する作用を有するタンパク質をコードすることにおいてのみ共通するものである。

しかしながら、文献 1 (JP 11-155581 A(岡本 尚)1999.06.15) には、NF  $\kappa$  B シグナルの活性制御に関わる新規蛋白質のアミノ酸配列、該蛋白質がコードするDNA配列、該DNAを有する形質転換体、該新規蛋白質に対する抗体、該DNAに対するアンチセンスについて、文献 2 (Li X, et. al., Proc. Natl. Ac ad. Sci. U.S.A. (2000 Sep), Vol. 97, No. 19, p. 10489-10493) には、NF- $\kappa$  B を活性化させる新規蛋白質Act1 について、文献 3 (Srinivasula SM, et. al., J. Biol. Chem. (1999), Vol. 274, No. 25, p. 17946-17954) には、NF- $\kappa$  B を活性化させる新規蛋白質CLAPについて記載されていることから、上記共通事項は先行技術の域をでるものではなく、「NF  $\kappa$  B を活性化する作用を有するタンパク質」はPCT規則 13. 2 における特別な技術的特徴であるとはいえない。

よって、配列番号1,3,5,7,9,11,・・,174,176,178または180のいずれかで表されるアミノ酸配列からなる90個の蛋白質は、単一の一般的発明概念を形成するように関連している一群の発明群であるとはいえず、異なった90個の蛋白質それぞれに関する90個の発明からなる発明群であると認める。

また、請求の範囲 13-15 に係る発明の「NF- $\kappa$ B活性化の阻害活性または促進活性について化合物をスクリーニングする方法」についても、上記共通事項である「NF $\kappa$ Bを活性化する作用を有するタンパク質」が先行技術の域を出るものではなく、PCT規則 13.2 における特別な技術特徴であるとは言えない以上、上記 90 個の発明群と単一の一般的発明概念を形成するように連関している一群の発明と認められないことから、第 91 の発明群を構成すると認める。

さらに、 請求の範囲 27は、上記特別な技術的特徴を有さず、第92の発明群を構成する。

それ故に請求の範囲の全てに共通の特別な技術事項はなく、上記発明群が単一の一般的な発明概念を形成するように連関している一群の発明であるとは認められない。

すなわち、請求の範囲には、

- (1) 請求の範囲1-11, 16-18, 24-26, 28-31のうち、配列番号1に関する部分
- (2) 請求の範囲1-11, 16-18, 24-26, 28-31のうち、配列番号 3 に関する部分
- (3) 請求の範囲1-11, 16-18, 24-26, 28-31のうち、配列番号 5 に関する部分
- (89) 請求の範囲1-11, 16-18, 24-26, 28-31のうち、配列番号178に関する部分
- (90) 請求の範囲1-11, 16-18, 24-26, 28-31のうち、配列番号180に関する部分
- (91) 請求の範囲13-15の NFーκB活性化の阻害活性または促進活性について化合物を スクリーニングする方法に関する部分
- (92) 請求の範囲27の機能をもつ新規完全長cDNAの取得方法に関する部分

の第92発明が記載されていると認められる。